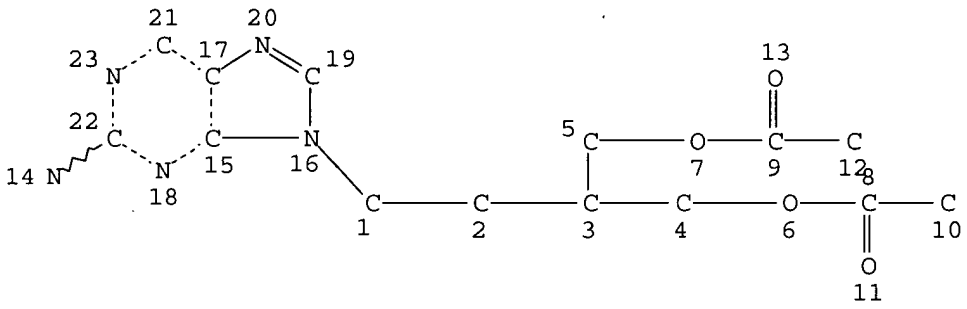
=> dis his

(FILE 'HOME' ENTERED AT 16:55:29 ON 11 AUG 2005)

FILE 'REGISTRY' ENTERED AT 16:55:37 ON 11 AUG 2005
E FAMCICLOVIR SOLVATE/CN
E FAMCICLOVIR/CN 5
L1 1 S E3
L2 STR 104227-87-4
L3 SCR 2127
L4 5 S L2 AND L3
L5 STR
L6 STR L5
L7 0 S L2 AND L6 AND L3
L8 2 S L2 AND L6 AND L3 FUL
L9 29 S L4 FUL
L10 2 SEARCH L6 SUB=L9 FUL

=> d l8 que stat;d 1-2 ide can;s l10 not l8
L2 STR



NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 23

STEREO ATTRIBUTES: NONE
L3 SCR 2127
L6 STR

G1—OH
1 2

VAR G1=ME/ET/I-PR/N-PR
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 2

STEREO ATTRIBUTES: NONE
L8 2 SEA FILE=REGISTRY SSS FUL L2 AND L6 AND L3

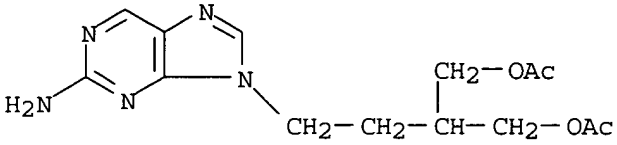
Prepared by: Mary Hale @2-2507 Rem Bldg 1D86

100.0% PROCESSED 43 ITERATIONS 2 ANSWERS
SEARCH TIME: 00.00.01

L10 ANSWER 1 OF 2 REGISTRY COPYRIGHT 2005 ACS on STN
RN 666832-89-9 REGISTRY
ED Entered STN: 24 Mar 2004
CN 1,3-Propanediol, 2-[2-(2-amino-9H-purin-9-yl)ethyl]-, diacetate (ester), compd. with ethanol (1:1) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Famciclovir ethanol solvate
MF C14 H19 N5 O4 . C2 H6 O
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

CM 1

CRN 104227-87-4
CMF C14 H19 N5 O4



CM 2

CRN 64-17-5
CMF C2 H6 O

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 140:235744

L10 ANSWER 2 OF 2 REGISTRY COPYRIGHT 2005 ACS on STN
RN 666832-88-8 REGISTRY
ED Entered STN: 24 Mar 2004
CN 1,3-Propanediol, 2-[2-(2-amino-9H-purin-9-yl)ethyl]-, diacetate (ester), compd. with methanol (1:1) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Famciclovir methanol solvate
MF C14 H19 N5 O4 . C H4 O
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

CM 1

Prepared by: Mary Hale @2-2507 Rem Bldg 1D86

CRN 104227-87-4
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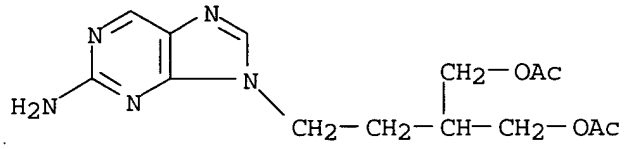

CM 2

CRN 67-56-1
CMF C H4 O

H_3C-OH

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 140:235744

L11 0 L10 NOT L8

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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	373.44	373.65

FILE 'CAPLUS' ENTERED AT 16:59:36 ON 11 AUG 2005

FILE COVERS 1907 - 11 Aug 2005 VOL 143 ISS 7
FILE LAST UPDATED: 10 Aug 2005 (20050810/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

Prepared by: Mary Hale @2-2507 Rem Bldg 1D86

L12 1 L10

=> d ibib abs hitstr

L12 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:182880 CAPLUS
DOCUMENT NUMBER: 140:235744
TITLE: Crystalline solid famciclovir forms I, II, III and preparation thereof
INVENTOR(S): Dolitzky, Ben-Zion; Wizel, Shlomit; Reany, Ofer; Shammai, Jenny
PATENT ASSIGNEE(S): Teva Pharmaceutical Industries Ltd., Israel; Teva Pharmaceuticals USA, Inc.
SOURCE: PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004018470	A2	20040304	WO 2003-US26875	20030826
WO 2004018470	A3	20040401		
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
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US 2004097528	A1	20040520	US 2003-649399	20030826
EP 1532151	A2	20050525	EP 2003-749164	20030826
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				

PRIORITY APPLN. INFO.:
US 2002-406173P P 20020826
US 2002-422243P P 20021029
WO 2003-US26875 W 20030826

AB The present invention provides novel crystalline solid anhydrous forms of famciclovir, denominated form I, II, and III, as well as their prepns. thereof by crystallization from organic solvents, and pharmaceutical compns. Thus, famciclovir (a mixture of crystalline solid famciclovir form I and form II) (3 g) was dissolved in a min. volume of CH2Cl2 while stirring. If necessary, the mixture was warmed for a short time until no precipitate was observed The solution was then cooled to room temperature and allowed to stand overnight. If required, the solution was left to stand for a longer period of time. The crystals (a substantially pure crystalline solid famciclovir form I) were filtered off and dried at 40° under vacuum.

IT **666832-88-8P**, Famciclovir methanol solvate **666832-89-9P**, Famciclovir ethanol solvate

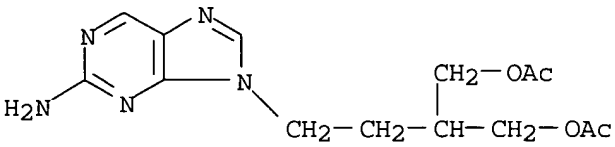
Prepared by: Mary Hale @2-2507 Rem Bldg 1D86

RL: PAC (Pharmacological activity); PEP (Physical, engineering or chemical process); PRP (Properties); PYP (Physical process); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(preparation of crystalline solid famciclovir forms I, II, III by crystallization from
organic solvents and/or water)

RN 666832-88-8 CAPLUS
CN 1,3-Propanediol, 2-[2-(2-amino-9H-purin-9-yl)ethyl]-, diacetate (ester), compd. with methanol (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 104227-87-4
CMF C14 H19 N5 O4



CM 2

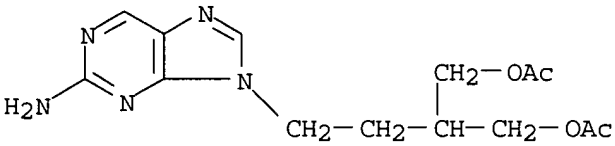
CRN 67-56-1
CMF C H4 O

H_3C-OH

RN 666832-89-9 CAPLUS
CN 1,3-Propanediol, 2-[2-(2-amino-9H-purin-9-yl)ethyl]-, diacetate (ester), compd. with ethanol (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 104227-87-4
CMF C14 H19 N5 O4



CM 2

CRN 64-17-5
CMF C2 H6 O

Substance data SEARCH and crossover from CAS REGISTRY in progress...
Use DISPLAY HITSTR (or FHITSTR) to directly view retrieved structures.

L14 434 L13

505 FAMCICLOVIR
8849 SOLVATE
4690 SOLVATES
12364 SOLVATE
(SOLVATE OR SOLVATES)
1 (L14 OR FAMCICLOVIR)(L)SOLVATE
181797 METHANOL
679 METHANOLS
182154 METHANOL
(METHANOL OR METHANOLS)
70497 PROPANOL
1588 PROPANOLS
71169 PROPANOL
(PROPANOL OR PROPANOLS)
231648 ETHANOL
1103 ETHANOLS
232187 ETHANOL
(ETHANOL OR ETHANOLS)
L15 1 (L14 OR FAMCICLOVIR)(L)SOLVATE AND (METHANOL OR PROPANOL OR ETHANOL)

=> d

L15 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:182880 CAPLUS
DN 140:235744
TI Crystalline solid famciclovir forms I, II, III and preparation thereof
IN Dolitzky, Ben-Zion; Wizel, Shlomit; Reany, Ofer; Shammai, Jenny
PA Teva Pharmaceutical Industries Ltd., Israel; Teva Pharmaceuticals USA, Inc.
SO PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004018470	A2	20040304	WO 2003-US26875	20030826
	WO 2004018470	A3	20040401		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,

Prepared by: Mary Hale @2-2507 Rem Bldg 1D86

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            FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
            BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
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     US 2004097528        A1    20040520    US 2003-649399         20030826
     EP 1532151           A2    20050525    EP 2003-749164         20030826
        R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
            IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
PRAI US 2002-406173P      P     20020826
     US 2002-422243P      P     20021029
     WO 2003-US26875      W     20030826


=> dis his

     (FILE 'HOME' ENTERED AT 16:55:29 ON 11 AUG 2005)

     FILE 'REGISTRY' ENTERED AT 16:55:37 ON 11 AUG 2005
               E FAMCICLOVIR SOLVATE/CN
               E FAMCICLOVIR/CN 5
L1             1 S E3
L2               STR 104227-87-4
L3               SCR 2127
L4             5 S L2 AND L3
L5               STR
L6               STR L5
L7             0 S L2 AND L6 AND L3
L8             2 S L2 AND L6 AND L3 FUL
L9            29 S L4 FUL
L10            2 SEARCH L6  SUB=L9 FUL
L11            0 S L10 NOT L8

     FILE 'CAPLUS' ENTERED AT 16:59:36 ON 11 AUG 2005
L12            1 S L10
               S ( 104227-87-4/REG# OR FAMCICLOVIR)(L)SOLVATE AND (METHANOL OR

     FILE 'REGISTRY' ENTERED AT 17:01:47 ON 11 AUG 2005
L13            1 S 104227-87-4/RN

     FILE 'CAPLUS' ENTERED AT 17:01:47 ON 11 AUG 2005
L14          434 S L13
L15            1 S ( L14 OR FAMCICLOVIR)(L)SOLVATE AND (METHANOL OR PROPANOL OR

=> del his y

=> fil reg
COST IN U.S. DOLLARS                            SINCE FILE      TOTAL
                                                   ENTRY    SESSION
FULL ESTIMATED COST                                12.89     393.71

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)      SINCE FILE      TOTAL
                                                   ENTRY    SESSION
CA SUBSCRIBER PRICE                                 0.00      -0.73

FILE 'REGISTRY' ENTERED AT 17:02:34 ON 11 AUG 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2005 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file

Prepared by: Mary Hale @2-2507 Rem Bldg 1D86
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=> fil reg
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                         0.43     703.45

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)              SINCE FILE      TOTAL
                                                           ENTRY    SESSION
CA SUBSCRIBER PRICE                                         0.00     -48.91

FILE 'REGISTRY' ENTERED AT 17:06:47 ON 11 AUG 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:   10 AUG 2005  HIGHEST RN 859511-21-0
DICTIONARY FILE UPDATES:  10 AUG 2005  HIGHEST RN 859511-21-0

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 18, 2005

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

**********************************************************************
*                                                                    *
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added,   *
* effective March 20, 2005.  A new display format, IDERL, is now    *
* available and contains the CA role and document type information. *
*                                                                    *
**********************************************************************

Structure search iteration limits have been increased.  See HELP SLIMITS
for details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=> e famciclovir monohydrate/cn 5
E1            1     FAMCICLOVIR ETHANOL SOLVATE/CN
E2            1     FAMCICLOVIR METHANOL SOLVATE/CN
E3            1 --> FAMCICLOVIR MONOHYDRATE/CN
E4            1     FAMCICLOVIR NITRATE/CN
E5            1     FAMCIN/CN

=> s e3
L1            1 "FAMCICLOVIR MONOHYDRATE"/CN

=> fil caplus;s l1/p
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                         5.03     708.48


Prepared by: Mary Hale @2-2507 Rem Bldg 1D86
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DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-48.91

FILE 'CAPLUS' ENTERED AT 17:07:06 ON 11 AUG 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 11 Aug 2005 VOL 143 ISS 7
FILE LAST UPDATED: 10 Aug 2005 (20050810/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

L2 3 L1/P

=> d 1-3 ibib abs hitstr

L2 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:182880 CAPLUS
DOCUMENT NUMBER: 140:235744
TITLE: Crystalline solid famciclovir forms I, II, III and preparation thereof
INVENTOR(S): Dolitzky, Ben-Zion; Wizel, Shlomit; Reany, Ofer; Shammai, Jenny
PATENT ASSIGNEE(S): Teva Pharmaceutical Industries Ltd., Israel; Teva Pharmaceuticals USA, Inc.
SOURCE: PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004018470	A2	20040304	WO 2003-US26875	20030826
WO 2004018470	A3	20040401		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

Prepared by: Mary Hale @2-2507 Rem Bldg 1D86

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2496684	AA	20040304	CA 2003-2496684	20030826
US 2004097528	A1	20040520	US 2003-649399	20030826
EP 1532151	A2	20050525	EP 2003-749164	20030826

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

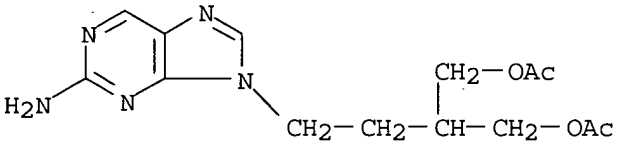
PRIORITY APPLN. INFO.:	US 2002-406173P	P	20020826
	US 2002-422243P	P	20021029
	WO 2003-US26875	W	20030826

AB The present invention provides novel crystalline solid anhydrous forms of famciclovir, denominated form I, II, and III, as well as their prepns. thereof by crystallization from organic solvents, and pharmaceutical compns. Thus, famciclovir (a mixture of crystalline solid famciclovir form I and form II) (3 g) was dissolved in a min. volume of CH2Cl2 while stirring. If necessary, the mixture was warmed for a short time until no precipitate was observed The solution was then cooled to room temperature and allowed to stand overnight. If required, the solution was left to stand for a longer period of time. The crystals (a substantially pure crystalline solid famciclovir form I) were filtered off and dried at 40° under vacuum.

IT **131118-73-5P**, Famciclovir monohydrate
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); SPN (Synthetic preparation); PREP (Preparation); PROC (Process)
(dehydration; preparation of crystalline solid famciclovir forms I, II, III by crystallization from organic solvents and/or water)

RN 131118-73-5 CAPLUS

CN 1,3-Propanediol, 2-[2-(2-amino-9H-purin-9-yl)ethyl]-, diacetate (ester), monohydrate (9CI) (CA INDEX NAME)



● H_2O

L2 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:	1997:542449 CAPLUS
DOCUMENT NUMBER:	127:210347
TITLE:	Pharmaceutical compositions containing famciclovir monohydrate
INVENTOR(S):	Campbell, Kenneth Churchill; Greenway, Michael John; Hancock, Stephen Andrew
PATENT ASSIGNEE(S):	Smithkline Beecham PLC, UK
SOURCE:	PCT Int. Appl., 9 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent

Prepared by: Mary Hale @2-2507 Rem Bldg 1D86

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9729108	A1	19970814	WO 1997-EP523	19970204
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
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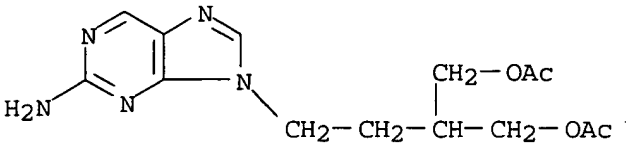
AU 9716013	A1	19970828	AU 1997-16013	19970204
EP 885223	A1	19981223	EP 1997-902336	19970204
EP 885223	B1	20010919		
R: BE, CH, DE, ES, FR, GB, IT, LI, NL				
JP 2000504679	T2	20000418	JP 1997-528144	19970204
ES 2165020	T3	20020301	ES 1997-902336	19970204
ZA 9700932	A	19980805	ZA 1997-932	19970205
HK 1016590	A1	20020412	HK 1999-101518	19990412
US 2003134864	A1	20030717	US 2000-735438	20001213
US 2005171124	A1	20050804	US 2004-980469	20041103

PRIORITY APPLN. INFO.:	GB 1996-2403	A	19960207
	GB 1996-18494	A	19960905
	WO 1997-EP523	W	19970204
	US 1998-117823	B1	19981202
	US 2000-735438	B2	20001213
	US 2004-757905	B1	20040115

AB A process for the preparation of famciclovir (I) monohydrate by exposing the anhydrous form to an atmospheric containing a high concentration of water vapor and pharmaceutical formulations containing I monohydrate are disclosed. Thus, 150 g I was dissolved in hot water and the hot solution was allowed to cool slowly to 5° with continuous stirring for 3 h. The monohydrate crystals were filtered and then dried by allowing the excess water to evaporate under ambient condition for .apprx.2 days. An oral suspension containing 35.20% I monohydrate was prepared and stored at 25° and the crystal growth was monitored and compared with a suspension containing anhydrous I over a period of 1 wk. No crystal growth in the monohydrate suspension was observed while the crystals in anhydrate suspension had grown to ten times their original size, making them less pharmaceutic ally acceptable.

IT **131118-73-5P**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(pharmaceutical compns. containing famciclovir monohydrate)

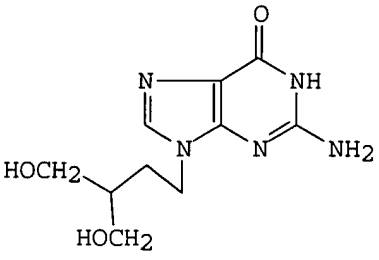
RN 131118-73-5 CAPLUS
CN 1,3-Propanediol, 2-[2-(2-amino-9H-purin-9-yl)ethyl]-, diacetate (ester), monohydrate (9CI) (CA INDEX NAME)



● H_2O

L2 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1991:24465 CAPLUS
DOCUMENT NUMBER: 114:24465
TITLE: Crystal and molecular structures of the antiviral acyclonucleoside 9-[4-hydroxy-3-(hydroxymethyl)butyl]guanine (BRL 39123, penciclovir) and its prodrug 9-[4-acetoxy-3-(acetoxymethyl)butyl]-2-aminopurine (BRL 42810, famciclovir)
AUTHOR(S): Harnden, Michael R.; Jarvest, Richard L.; Slawin, Alexandra M. Z.; Williams, David J.
CORPORATE SOURCE: Biosci. Res. Cent., Beecham Pharm. Res. Div., Epsom/Surrey, KT18 5XQ, UK
SOURCE: Nucleosides & Nucleotides (1990), 9(4), 499-513
CODEN: NUNUD5; ISSN: 0732-8311
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



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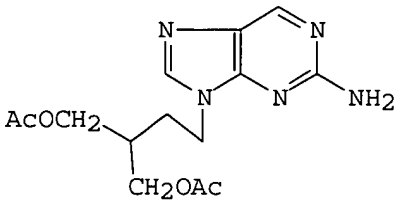
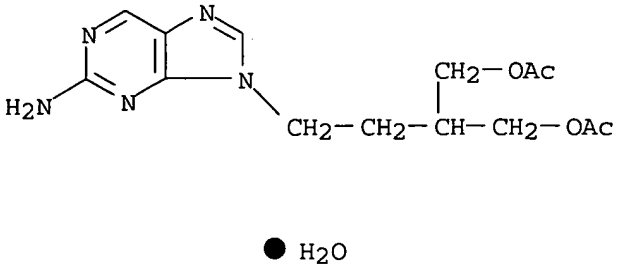


II

AB The crystal and mol. structures of acyclonucleosides related antiviral purine derivs. are reported. In I the plane of the acyclic N9 substituent is orthogonal to the purine ring, and there is an intermol. hydrogen bonds. In II characteristic changes in the geometry of the pyrimidine ring in comparison with I are observed In crystals of II there is an absence of major hydrogen bonding interactions and there are π-π interactions between parallel overlapping pyrimidine moieties.

IT **131118-73-5P**
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(preparation and crystal structure of)
RN 131118-73-5 CAPLUS
CN 1,3-Propanediol, 2-[2-(2-amino-9H-purin-9-yl)ethyl]-, diacetate (ester), monohydrate (9CI) (CA INDEX NAME)



● H_2O

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=> s (l1 or 13118-73-5 or famciclovir monohydrate)(l)(prep? or crystal?)
   REGlstRY INITIATED
Substance data SEARCH and crossover from CAS REGISTRY in progress...
Use DISPLAY HITSTR (or FHITSTR) to directly view retrieved structures.

L4            0 L3


              3 L1
            505 FAMCICLOVIR
          24763 MONOHYDRATE
            778 MONOHYDRATES
          25249 MONOHYDRATE
                  (MONOHYDRATE OR MONOHYDRATES)
              2 FAMCICLOVIR MONOHYDRATE
                  (FAMCICLOVIR(W)MONOHYDRATE)
        4618870 PREP?
        1673077 CRYSTAL?
         331069 CRYST
           1798 CRYSTS
         332336 CRYST
                  (CRYST OR CRYSTS)
          86745 CRYSTD
          17808 CRYSTG
         223743 CRYSTN
           2314 CRYSTNS
         225028 CRYSTN
                  (CRYSTN OR CRYSTNS)
        1963105 CRYSTAL?
                  (CRYSTAL? OR CRYST OR CRYSTD OR CRYSTG OR CRYSTN)
L5            3 (L1 OR L4 OR FAMCICLOVIR MONOHYDRATE)(L)(PREP? OR CRYSTAL?)


=> s l5 not l2
L6            0 L5 NOT L2

=> dis his

     (FILE 'CAPLUS' ENTERED AT 17:04:33 ON 11 AUG 2005)
                DEL HIS Y
```

Prepared by: Mary Hale @2-2507 Rem Bldg 1D86

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     FILE 'REGISTRY' ENTERED AT 17:06:34 ON 11 AUG 2005

     FILE 'REGISTRY' ENTERED AT 17:06:47 ON 11 AUG 2005
                E FAMCICLOVIR MONOHYDRATE/CN 5
L1             1 S E3

     FILE 'CAPLUS' ENTERED AT 17:07:06 ON 11 AUG 2005
L2             3 S L1/P
                 S (L1 OR  13118-73-5/REG# OR FAMCICLOVIR MONOHYDRATE)(L)(PREP?

     FILE 'REGISTRY' ENTERED AT 17:07:54 ON 11 AUG 2005
L3             0 S 13118-73-5/RN

     FILE 'CAPLUS' ENTERED AT 17:07:55 ON 11 AUG 2005
L4             0 S L3
L5             3 S (L1 OR L4 OR FAMCICLOVIR MONOHYDRATE)(L)(PREP? OR CRYSTAL?)
L6             0 S L5 NOT L2

=> log y
COST IN U.S. DOLLARS                            SINCE FILE      TOTAL
                                                   ENTRY    SESSION
FULL ESTIMATED COST                                 9.90     734.08

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)      SINCE FILE      TOTAL
                                                   ENTRY    SESSION
CA SUBSCRIBER PRICE                                 0.00     -51.10

STN INTERNATIONAL LOGOFF AT 17:08:28 ON 11 AUG 2005
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=> e famiciclovir/cn 5
E1            1     FAMEX P 18/CN
E2            1     FAMFUR/CN
E3            0 --> FAMICICLOVIR/CN
E4            1     FAMICIDIN/CN
E5            1     FAMID/CN

=> e famciclovir/cn 5
E1            1     FAMATINITE, ARSENIAN FERROAN STANNIAN ((SB0.5-0.8AS0.1-0.4SN
                    0.1-0.4)CU2(CU0.6-0.9FE0.1-0.4)S4)/CN
E2            1     FAMATINITE, SELENIAN SBCU3(S0.5-0.9SE0.1-0.5)4/CN
E3            1 --> FAMCICLOVIR/CN
E4            1     FAMCICLOVIR ETHANOL SOLVATE/CN
E5            1     FAMCICLOVIR METHANOL SOLVATE/CN

=> s e3
L1            1 FAMCICLOVIR/CN

=> fil caplus;s (l1 or famciclovir or 104227-87-4)(l)(prep? or crys? or crystal?)
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                   ENTRY    SESSION
FULL ESTIMATED COST                                 5.46     399.17

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)    SINCE FILE      TOTAL
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CA SUBSCRIBER PRICE                                 0.00      -0.73

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FILE COVERS 1907 - 11 Aug 2005  VOL 143 ISS 7
FILE LAST UPDATED: 10 Aug 2005  (20050810/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.

   REGlstRY INITIATED
Substance data SEARCH and crossover from CAS REGISTRY in progress...
Use DISPLAY HITSTR (or FHITSTR) to directly view retrieved structures.
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Prepared by: Mary Hale @2-2507 Rem Bldg 1D86

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L3          434 L2


            434 L1
            505 FAMCICLOVIR
        4618870 PREP?
        1964655 CRYS?
        1673077 CRYSTAL?
         331069 CRYST
           1798 CRYSTS
         332336 CRYST
                  (CRYST OR CRYSTS)
          86745 CRYSTD
          17808 CRYSTG
         223743 CRYSTN
           2314 CRYSTNS
         225028 CRYSTN
                  (CRYSTN OR CRYSTNS)
        1963105 CRYSTAL?
                  (CRYSTAL? OR CRYST OR CRYSTD OR CRYSTG OR CRYSTN)
L4           71 (L1 OR FAMCICLOVIR OR L3 )(L)(PREP? OR CRYS? OR CRYSTAL?)


=> fil reg
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
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FULL ESTIMATED COST                                     9.90     409.95

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                       ENTRY    SESSION
CA SUBSCRIBER PRICE                                     0.00      -0.73

FILE 'REGISTRY' ENTERED AT 17:04:13 ON 11 AUG 2005
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Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:   10 AUG 2005  HIGHEST RN 859511-21-0
DICTIONARY FILE UPDATES:  10 AUG 2005  HIGHEST RN 859511-21-0

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 18, 2005

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

**********************************************************************
*                                                                    *
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added,   *
* effective March 20, 2005.  A new display format, IDERL, is now    *
* available and contains the CA role and document type information. *
*                                                                    *

Prepared by: Mary Hale @2-2507 Rem Bldg 1D86
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Structure search iteration limits have been increased. See HELP SLIMITS for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

```
=> e famciclovir hydrate/cn 5
E1            1     FAMCICLOVIR/CN
E2            1     FAMCICLOVIR ETHANOL SOLVATE/CN
E3            0 --> FAMCICLOVIR HYDRATE/CN
E4            1     FAMCICLOVIR METHANOL SOLVATE/CN
E5            1     FAMCICLOVIR MONOHYDRATE/CN

=> fil caplus
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                                                   ENTRY    SESSION
FULL ESTIMATED COST                                 0.43     410.38

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)      SINCE FILE      TOTAL
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CA SUBSCRIBER PRICE                                 0.00      -0.73

FILE 'CAPLUS' ENTERED AT 17:04:33 ON 11 AUG 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2005 AMERICAN CHEMICAL SOCIETY (ACS)
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FILE COVERS 1907 - 11 Aug 2005  VOL 143 ISS 7
FILE LAST UPDATED: 10 Aug 2005  (20050810/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.

=> s l4 not ?hydrate?
        440148 ?HYDRATE?
L5          66 L4 NOT ?HYDRATE?

=> d 1-66 ibib abs hitstr

L5   ANSWER 1 OF 66  CAPLUS  COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:         2005:395106  CAPLUS
DOCUMENT NUMBER:          142:447233

Prepared by: Mary Hale @2-2507 Rem Bldg 1D86
```

TITLE: Preparation of heterocycle-substituted pteridine derivatives as immunosuppressants

INVENTOR(S): Waer, Mark Jozef Albert; Herdewijn, Piet Andre Maurits Maria; De Jonghe, Steven Cesar Alfons; Marchand, Arnaud Didier Marie; Gao, Ling-Jie

PATENT ASSIGNEE(S): 4 Aza Bioscience NV, Belg.

SOURCE: PCT Int. Appl., 117 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 7

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2005039587	A1	20050506	WO 2004-EP11836		20041018
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
GB 2407089	A1	20050420	GB 2003-24324		20031017
PRIORITY APPLN. INFO.:			GB 2003-24324	A	20031017
			GB 2004-8955	A	20040422

OTHER SOURCE(S): MARPAT 142:447233

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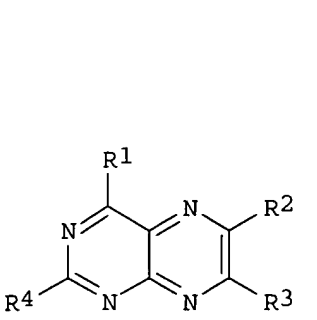

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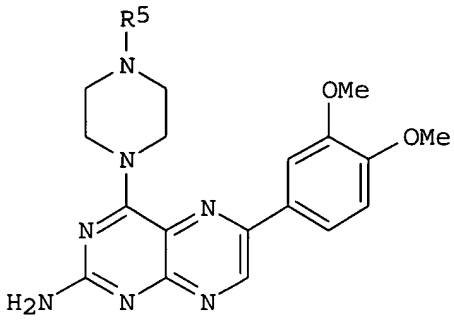

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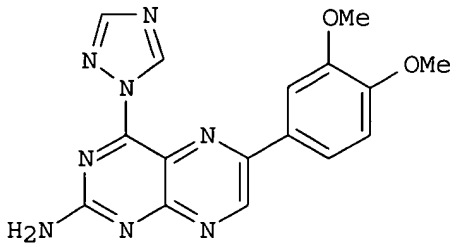


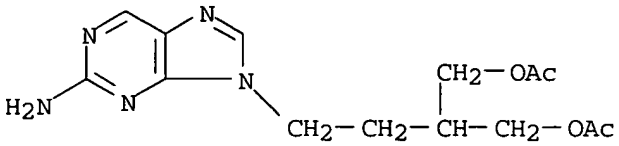
III

AB The invention relates to the preparation of novel pteridine derivs. of formula I [wherein: one or more of R1-R4 is independently selected from (un)substituted saturated or partly saturated heterocyclic 5-7-membered rings], their pharmaceutically acceptable salts, and/or stereoisomers, N-oxides, solvates, dihydro- and tetrahydropteridine derivative, useful as immunosuppressants in the treatment of transplant rejection and inflammatory diseases. The invention relates to the treatment of toxic side effects, disorders, and diseases related to or resulting from the exposure of patients to abnormally high level of TNF-α. I are also useful in preventing or treating cardiovascular disorders, allergic conditions, disorders of the central nervous system, TNF-α related disorders, viral diseases and cell proliferative disorders. For instance, pteridine derivative II [R5 = C(O)Me; TNF-α assay: IC50 = 0.4 μM; mixed lymphocyte reaction assay: IC50 = 0.9 μmole/L] was prepared via substitution of the triazole ring of triazolylpteridine derivative III by piperazine and subsequent N-acetylation of the obtained piperazinylpteridine derivative (yield: substitution - 85%). A model of TNF-α induced shock was performed with 80% survival rate of mice that received the pteridine derivative II (R5 is phenoxyacetyl).

IT **104227-87-4, Famciclovir**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(drug component; **preparation** of heterocycle-substituted pteridine derivs. useful as immunosuppressants)

RN 104227-87-4 CAPLUS

CN 1,3-Propanediol, 2-[2-(2-amino-9H-purin-9-yl)ethyl]-, diacetate (ester) (9CI) (CA INDEX NAME)



REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 2 OF 66 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:369255 CAPLUS
DOCUMENT NUMBER: 142:397782
TITLE: Aqueous aerosol preparation as inhalants for drugs with unpleasant sensory characteristics containing nonionic surfactants and phospholipids
INVENTOR(S): Jauernig, Juergen; Lintz, Frank-Christophe; Keller, Manfred
PATENT ASSIGNEE(S): Pari GmbH, Germany
SOURCE: PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

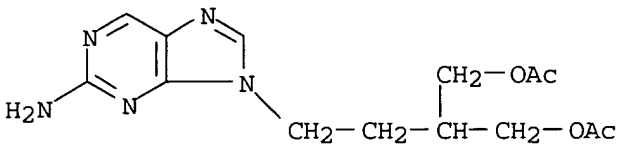
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005037246	A2	20050428	WO 2004-EP11571	20041014
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10347994	A1	20050616	DE 2003-10347994	20031015
PRIORITY APPLN. INFO.:			DE 2003-10347994 A	20031015

AB Disclosed are sterile aqueous prepns. that are to be inhaled as an aerosol and contain an active substance, a nonionic surfactant, and a phospholipid. Said prepns. are suitable for administering poorly soluble active substances by way of inhalation in the form of colloidal solns. and can also be used for administering bad-tasting active substances that irritate the mucus and cause cough or bronchoconstrictions. The inventive prepns. can be nebulized by means of conventional devices and are preferably used in pediatrics. Thus a 1000 mL aqueous formulation contained (g): Budesonide 0.2; Tyloxapol 10.0; DMPC 5.0; sodium chloride 8.4; citric acid/sodium acetate to pH 4.4.

IT **104227-87-4, Famciclovir**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(aqueous aerosol **preparation** as inhalants for drugs with unpleasant sensory characteristics containing nonionic surfactants and phospholipids)
RN 104227-87-4 CAPLUS
CN 1,3-Propanediol, 2-[2-(2-amino-9H-purin-9-yl)ethyl]-, diacetate (ester)

Prepared by: Mary Hale @2-2507 Rem Bldg 1D86

(9CI) (CA INDEX NAME)



L5 ANSWER 3 OF 66 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:335902 CAPLUS
DOCUMENT NUMBER: 142:392439
TITLE: A preparation of pteridine derivatives, useful as immunosuppressants
INVENTOR(S): Herdewijn, Piet; Waer, Mark; De Jonghe, Steven Cesar Alfons; Marchand, Arnaud Didier Marie
PATENT ASSIGNEE(S): 4 Aza Bioscience N. V., Belg.
SOURCE: Brit. UK Pat. Appl., 105 pp.
CODEN: BAXXDU
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 2407089	A1	20050420	GB 2003-24324	20031017
WO 2005039587	A1	20050506	WO 2004-EP11836	20041018

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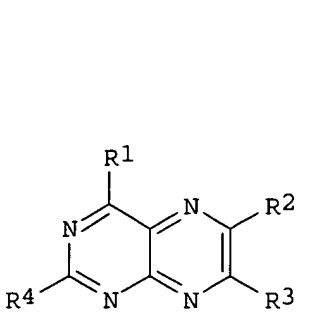
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: GB 2003-24324 A 20031017
GB 2004-8955 A 20040422
OTHER SOURCE(S): MARPAT 142:392439
GI



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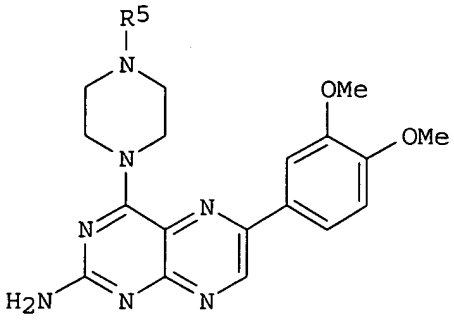

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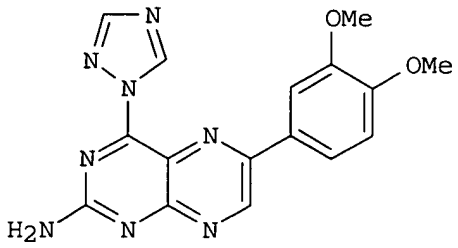


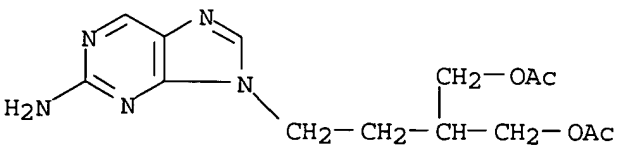
III

AB The invention relates to a preparation of novel pteridine derivs. of formula I [wherein: one or more of R1-R4 is independently selected from heterocyclic 5-7-membered rings], useful as immunosuppressants. The invention compds. are immunosuppressive agents and they are useful in treatment of transplant rejection and inflammatory diseases. The invention relates to the treatment of toxic side effects, disorders, and diseases related to or resulting from the exposure of patients to abnormally high level of TNF-α. For instance, pteridine derivative II [R5 = C(O)Me; TNF-α assay: IC50 = 0.4 μM; mixed lymphocyte reaction assay: IC50 = 0.9 μmole/L] was prepared via substitution of the triazole ring of triazolylpteridine derivative III by piperazine and subsequent N-acetylation of the obtained piperazinylpteridine derivative (yield: substitution - 85%). A model of TNF-α induced shock was performed with 80% survival rate of mice that received the pteridine derivative II (R5 is phenoxyacetyl).

IT **104227-87-4, Famciclovir**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(drug component; **preparation** of pteridine derivs. useful as immunosuppressants)

RN 104227-87-4 CAPLUS

CN 1,3-Propanediol, 2-[2-(2-amino-9H-purin-9-yl)ethyl]-, diacetate (ester) (9CI) (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS

Prepared by: Mary Hale @2-2507 Rem Bldg 1D86

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

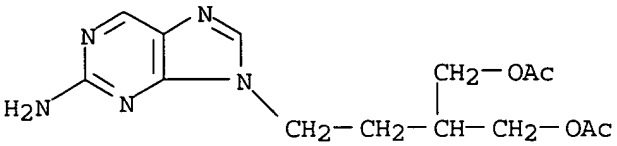
L5 ANSWER 4 OF 66 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:260069 CAPLUS
DOCUMENT NUMBER: 142:316618
TITLE: **Preparation** of **famciclovir**
INVENTOR(S): Shamai, Genny; Antebi, Shlomo; Ioffe, David; Dolitzky, Ben-Zion; Kauffmann, Batia
PATENT ASSIGNEE(S): Teva Pharmaceutical Industries Ltd., Israel; Teva Pharmaceuticals USA, Inc.
SOURCE: PCT Int. Appl., 15 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005026167	A1	20050324	WO 2004-US28489	20040902
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2005143400	A1	20050630	US 2004-932120	20040902
EP 1556383	A1	20050727	EP 2004-782892	20040902
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				

PRIORITY APPLN. INFO.: US 2003-500575P P 20030904
WO 2004-US28489 W 20040902
OTHER SOURCE(S): CASREACT 142:316618

AB The invention provides a process for making **famciclovir**, comprising reacting 9-[4-acetoxy-3-(acetoxymethyl)but-1-yl]-2-amino-6-chloropurine (Cl-FMC) with a palladium on charcoal catalyst in water and ammonium formate. The invention also provides methods of treating viral diseases by administering the title compound **prepared** according to the above process.

IT **104227-87-4P**, **Famciclovir**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**preparation** of **famciclovir** for treating herpes zoster, genital herpes, or mucocutaneous herpes simplex)
RN 104227-87-4 CAPLUS
CN 1,3-Propanediol, 2-[2-(2-amino-9H-purin-9-yl)ethyl]-, diacetate (ester) (9CI) (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 5 OF 66 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:107011 CAPLUS
DOCUMENT NUMBER: 142:442878
TITLE: Construction of herpes virus thymidine kinase mutant with improved phosphorylation ability to nucleotide analogs and uses in antitumor gene therapy
INVENTOR(S): Zhu, Jingde; Wang, Xiaomei
PATENT ASSIGNEE(S): New Century Gene Technology Development Co., Ltd., Shanghai, Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 28 pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1464051	A	20031231	CN 2002-111956	20020605
PRIORITY APPLN. INFO.:			CN 2002-111956	20020605

AB The thymidine kinase mutant of herpes virus, which shows higher phosphorylation ability to nucleotide analogs than the wild-type one, contains a mutation at position 152 of amino acid sequence. When the amino acid residue at position 152 of the mutant is Val, the amino acid residues at positions 168 and 169 are not Tyr and Phe. The nucleotide analog is ganciclovir, aciclovir, **famciclovir**, trifluridine, 2'-deoxy-2'-fluoro-β-D-arabinofuranosyl-5- iodouracil, araA, 2-β-D-arabinofuranosylthymine, 5-ethyl-2'- deoxyuridine, 5'-amino-5-iodo-2',5'-dideoxyuridine, AZT, AIU, dideoxycytidine, araC, etc. The thymidine kinase-coding nucleotide sequence or its recombinant expression vector may be used to **prepare** the nucleotide analog-dependent antitumor medical **prepns.**

L5 ANSWER 6 OF 66 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:1124561 CAPLUS
DOCUMENT NUMBER: 142:56088
TITLE: Process for the **preparation** of 2-amino-9-(2-substituted-ethyl)purines and 9-[4-acetoxy-3-(acetoxymethyl)but-1-yl]-2-aminopurine (**famciclovir**)
INVENTOR(S): Lee, Byoung-Suk; Shin, Sang-Hoon; Park, Jong-Sik
PATENT ASSIGNEE(S): Kyungdong Pharm. Co., Ltd., S. Korea
SOURCE: PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004110343	A2	20041223	WO 2004-KR1405	20040612

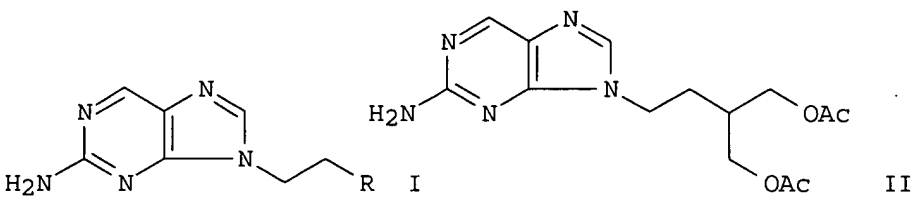
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: KR 2003-38417 A 20030613

OTHER SOURCE(S): CASREACT 142:56088; MARPAT 142:56088

GI

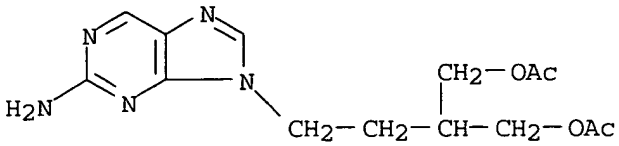


AB The present invention relates to a process for **preparing** of 2-amino-9-(2-substituted-ethyl)purines, such as I [R = OH, OSO2Me, OSO2C6H4-4-Me, halogen], and an effective method for **preparing** 9-[4-acetoxy-3-(acetoxymethyl)but-1-yl]-2-aminopurin (**famciclovir**) (II). The inventive method for the **preparation** of II comprised the steps of halogenating alc. I (R = OH) to give 2-amino-9-(2-haloethyl)purine I (R = halogen), reacting the halogenated compound with di-Et malonate, reduction of the dicarboxylate, and diacetylation of the resulting diol. The inventive **preparation** method allows II, a purine derivative drug with effective antiviral activity, to be **prepared** in a high selectivity of 100% in a pure form by using the intermediate purines I. In addition, the inventive method allows the utilization of relatively mild reaction conditions, and thus, has high industrial process efficiency.

IT **104227-87-4P**, 9-[4-Acetoxy-3-(acetoxymethyl)but-1-yl]-2-aminopurine
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(process for **preparation** of 2-amino-9-(2-substituted-ethyl)purines and 9-[4-acetoxy-3-(acetoxymethyl)but-1-yl]-2-aminopurine (**famciclovir**))

RN 104227-87-4 CAPLUS

CN 1,3-Propanediol, 2-[2-(2-amino-9H-purin-9-yl)ethyl]-, diacetate (ester) (9CI) (CA INDEX NAME)



L5 ANSWER 7 OF 66 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:1016008 CAPLUS
DOCUMENT NUMBER: 142:6507
TITLE: Preparation of naphthyridine integrase inhibitors
INVENTOR(S): Johns, Brian A.
PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA
SOURCE: PCT Int. Appl., 154 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004101512	A2	20041125	WO 2004-US14814	20040512
WO 2004101512	A3	20050127		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-470059P P 20030513
OTHER SOURCE(S): MARPAT 142:6507
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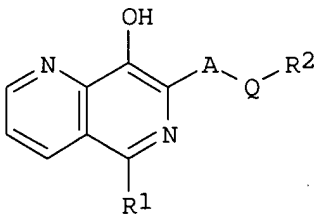


I

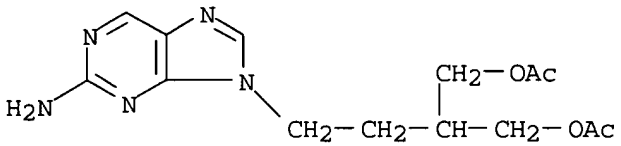
AB The title compds. [I; R1 = H, halo, alkyl, etc.; R2 = cycloalkyl, (un)substituted aryl, heterocyclyl; A = heterocycle; Q = alkyl, O, CO, SO2, etc.] that are HIV integrase inhibitors and therefore are useful in the inhibition of HIV replication, the prevention and/or treatment of infection by HIV, and in the treatment of AIDS and/or ARC, were prepared E.g., a multi-step synthesis of 7-(5-benzyl-4H-1,2,4-triazol-3-yl)-1,6-

naphthyridin-8-ol, was given. The compds. I have anti-HIV activity in the range IC50 of 1-1000 nM. The pharmaceutical composition comprising the compound I is disclosed.

IT **104227-87-4, Famciclovir**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(co-drug; **preparation** of naphthyridine integrase inhibitors for treating HIV infection in combination with other therapeutic agents)

RN 104227-87-4 CAPLUS

CN 1,3-Propanediol, 2-[2-(2-amino-9H-purin-9-yl)ethyl]-, diacetate (ester) (9CI) (CA INDEX NAME)



L5 ANSWER 8 OF 66 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:996181 CAPLUS
DOCUMENT NUMBER: 141:411197
TITLE: Process for the **preparation** of **famciclovir**
INVENTOR(S): Shamai, Genny; Antebi, Shlomo; Ioffe, David; Dolitzky, Ben-Zion; Kauffmann, Batia
PATENT ASSIGNEE(S): Teva Pharmaceutical Industries Ltd., Israel; Teva Pharmaceuticals USA, Inc.
SOURCE: PCT Int. Appl., 19 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004099208	A1	20041118	WO 2004-US13427	20040430
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004266795	A1	20041230	US 2004-836028	20040430
EP 1511750	A1	20050309	EP 2004-751022	20040430
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				

PRIORITY APPLN. INFO.:
US 2003-466705P P 20030430
US 2003-488268P P 20030716
WO 2004-US13427 W 20040430

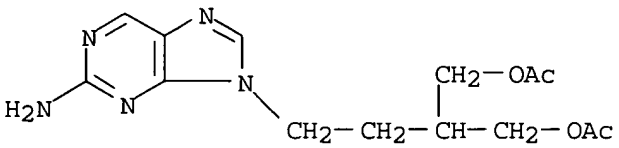
OTHER SOURCE(S): CASREACT 141:411197

AB The invention provides processes for making famciclovir with low levels of undesirable byproducts. The present invention discloses a process comprises reacting acetic acid 2-acetoxymethyl-4-(5-amino-7-chloro-imidazo[4,5-b]pyridin-3-yl)butyl ester (I) in the presence of a palladium on charcoal catalyst in a C1-C6 alkyl acetate and ammonium formate. The present invention further discloses a process comprises reacting I in the presence of a palladium on charcoal catalyst in a mixture of a C1-C6 alkyl acetate, a C1-C4 alc. and ammonium formate.

IT **104227-87-4P**, **Famciclovir**
RL: IMF (Industrial manufacture); PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(**preparation** and stability of **famciclovir**)

RN 104227-87-4 CAPLUS

CN 1,3-Propanediol, 2-[2-(2-amino-9H-purin-9-yl)ethyl]-, diacetate (ester) (9CI) (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 9 OF 66 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:534204 CAPLUS

DOCUMENT NUMBER: 141:89006

TITLE: Preparation of pyrrolidine and azetidine compounds as CCR5 antagonists

INVENTOR(S): Yang, Hanbiao; Kazmierski, Wieslaw Mieczyslaw; Aquino, Christopher Joseph

PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA

SOURCE: PCT Int. Appl., 130 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004055016	A1	20040701	WO 2003-US39618	20031212

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2002-433372P P 20021213

OTHER SOURCE(S): MARPAT 141:89006

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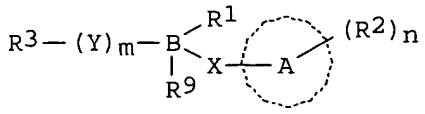

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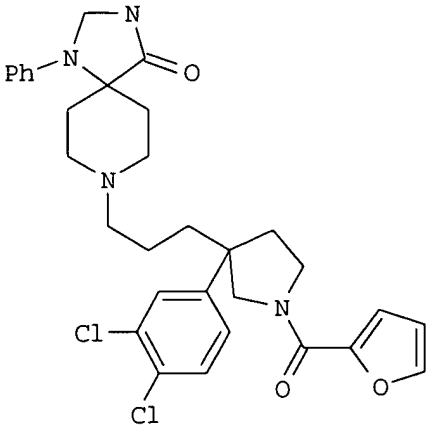
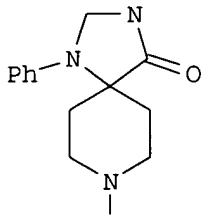


II



III

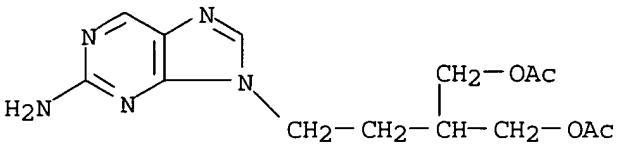
AB Title compds. I [R1 = (un)substituted-alkyl, -alkynyl, -cycloalkyl, -heterocyclyl, etc., or R1 and X taken together form a saturated, partially saturated or aromatic 5-6 membered ring having 0-3 heteroatoms selected from O, P, S, or N that is fused to ring A; R2 = OH, halogen (un)substituted-alkyl, -alkoxy, -aryl, -heteroaryl, -cycloalkyl, etc., or two geminal R2s are optionally taken together to from a spiro, saturated, partially saturated or aromatic 5-6 membered ring having 0-3 heteroatoms selected from O, P, S, or N, said fused or spiro ring optionally substituted; R3 = H, halo, cyano, trifluoromethyl, (un)substituted amino, acylamino, alkyl; R9 = H or oxo; X = C1-5 alkylene, optionally substituted with oxo, thioxo, -S(O)t where t = 1 or 2, halogen atoms, or alkyl and optionally containing 1-3 oxygen, nitrogen, sulfur, or phosphorus atoms; Y = carbonyl, thiocarbonyl, 1,2-dioxoethylene, alkyl, alkenyl, etc.; A = saturated, partially saturated, or aromatic 3-7 monocyclic or 8-10 membered bicyclic ring having one ring nitrogen and 0-4 addnl. heteroatoms selected from O, P, S or N; m = 0 or 1, n = 0-5;] and their pharmaceutically acceptable salts are prepared and disclosed as CCR5 antagonists. Thus, II was prepared via condensation of tert-Bu 3-(3,4-dichlorophenyl)-3-(3-oxopropyl)pyrrolidne-1-carboxylate (preparation given) with the amine III followed by deprotection and acylation with 2-furanoyl chloride. I have pIC50 values of ≥5 in assays for CCR5 antagonism. As CCR5 antagonists, I are useful for the treatment of viral infections (particularly HIV infection).

IT **104227-87-4**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug for therapeutic administration; **preparation** of pyrrolidine and azetidine derivs. as CCR5 antagonists)

RN 104227-87-4 CAPLUS

CN 1,3-Propanediol, 2-[2-(2-amino-9H-purin-9-yl)ethyl]-, diacetate (ester) (9CI) (CA INDEX NAME)

Prepared by: Mary Hale @2-2507 Rem Bldg 1D86



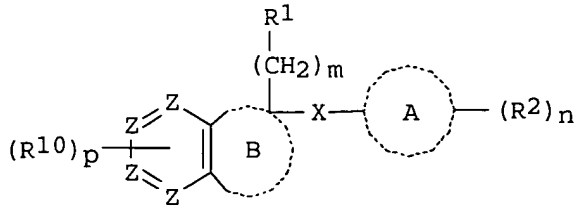
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 10 OF 66 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:534200 CAPLUS
DOCUMENT NUMBER: 141:88928
TITLE: Preparation of indane compounds and analogs as CCR5 antagonists
INVENTOR(S): Youngman, Michael; Kazmierski, Wieslaw Mieczyslaw; Yang, Hanbiao; Aquino, Christopher Joseph
PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA
SOURCE: PCT Int. Appl., 129 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004055012	A1	20040701	WO 2003-US39975	20031212

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2002-433378P P 20021213
OTHER SOURCE(S): MARPAT 141:88928
GI



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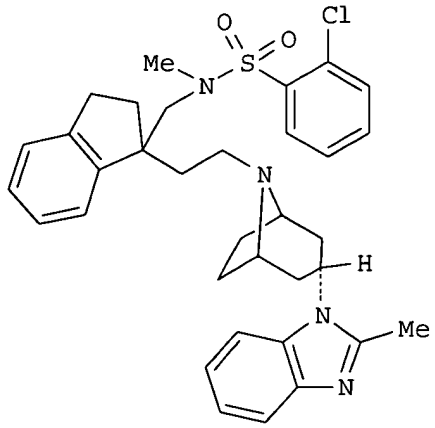


II

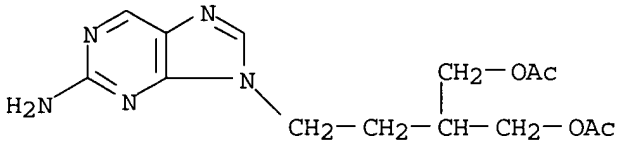
AB Title compds. I [R1 = (un)substituted saturated, partially saturated, or aromatic 4-7 monocyclic or 8-10 membered bicyclic ring having one ring N and 0-4 addnl. heteroatoms selected from O, P, S or N, optionally attached through alkylene chain, (un)substituted-amide, etc.; R2 = OH, (un)substituted-alkyl, -alkoxy, -heteroaryl, etc., optionally two adjacent R2s taken together form a fused, saturated, partially saturated or aromatic 5-6 membered ring having 0-3 heteroatoms selected from O, P, S, or N, or two geminal R2s optionally taken together from a spiro, saturated, partially saturated or aromatic 5-6 membered ring having 0-3 heteroatoms selected from O, P, S or N, said fused or spiro ring being optionally substituted; R10 = H, halo, F3C, (un)substituted-aryl, etc., or two R10s may together form a 3-7 membered saturated, partially saturated, or aromatic carbocyclic ring, optionally containing one or more heteroatom selected from O, P, N, or S that is fused to depicted ring; X = (un)substituted-alkylene chain which optionally may have 0-3 heteroatoms selected from O, P, S or N; A = saturated, partially saturated, or aromatic 3-7 monocyclic or 8-10 membered bicyclic ring having one ring nitrogen and 0-4 addnl. heteroatoms selected from O, P, S or N ; B = 4-7 membered saturated, partially saturated, or aromatic carbocyclic ring optionally containing 1-2 heteroatoms selected from O, P, S, or N; each Z maybe C or N (at least one Z = C) ; m = 1-3, n = 0-5, p = 0-4] and their pharmaceutically acceptable salts are prepared and disclosed as CCR5 antagonists. Thus, II was prepared by reaction of N-methyl(1-{2-[(1R,5S)-3-(2-methyl-1H-benzimidazol-1-yl)-8-azabicyclo[3.2.1]oct-8-yl]ethyl}-2,3-dihydro-1H-inden-1-yl)methanamine (preparation given) with 2-chlorophenylsulfonyl chloride. A preparative example utilizing

combinatorial methods of synthesis is provided. I have pIC50 values of ≥5 in assays for CCR5 antagonism. As CCR5 antagonists, I are useful for the treatment of viral infections (particularly HIV infection).

IT **104227-87-4**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug for therapeutic administration; **preparation** of indane compds. and analogs as CCR5 antagonists)

RN 104227-87-4 CAPLUS

CN 1,3-Propanediol, 2-[2-(2-amino-9H-purin-9-yl)ethyl]-, diacetate (ester) (9CI) (CA INDEX NAME)



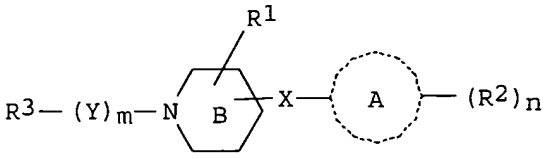
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 11 OF 66 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:534199 CAPLUS
DOCUMENT NUMBER: 141:89094
TITLE: Preparation of oxazine and morpholine derivatives as CCR5 antagonists
INVENTOR(S): Aquino, Christopher Joseph; Chong, Pek Yong; Duan, Maosheng; Kazmierski, Wieslaw Mieczyslaw
PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA
SOURCE: PCT Int. Appl., 106 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004055011	A1	20040701	WO 2003-US39740	20031212

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2002-433410P P 20021213
OTHER SOURCE(S): MARPAT 141:89094
GI



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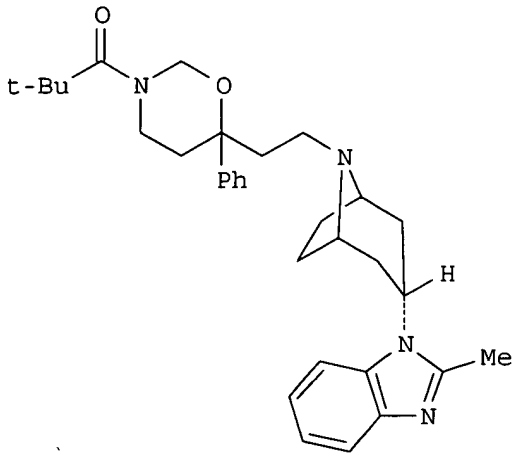


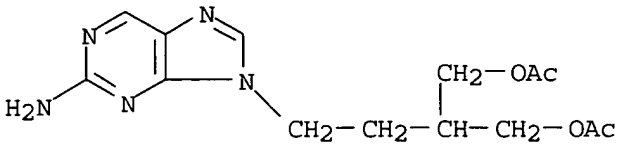
II

AB Title compds. I [R1 = (un)substituted-alkyl, -alkenyl, -alkynyl, -cycloalkyl, etc., or R1 and X taken together from a saturated, partially saturated, or aromatic 5-6 membered ring having 0-3 heteroatoms selected from O, P, S or N fused to ring A; R2 = OH, halo, (un)substituted-alkyl, -alkynyl, -heteroaryl, etc., optionally two adjacent R2s taken together form a fused, saturated, partially saturated or aromatic 5-6 membered ring having 0-3 heteroatoms selected from O, P, S, or N, or two geminal R2s optionally taken together from a (un)substituted spiro, saturated, partially saturated or aromatic 5-6 membered ring having 0-3 heteroatoms selected from O, P, S or N, said fused or spiro ring being optionally substituted; X = (un)substituted-alkylene chain which optionally may have 0-3 heteroatoms selected from O, P, S or N; A = saturated, partially saturated, or aromatic 3-7 monocyclic or 8-10 membered bicyclic ring having one ring nitrogen and 0-4 addnl. heteroatoms selected from O, P, S or N ; Ring B contains an oxygen atom in addition to depicted N; R3 = H, amine, CF3, halo, (un)substituted alkyl, etc., Y = alkyl, alkenyl, alkynyl, carbonyl, thiocarbonyl, etc.; m = 0-1, n = 0-5] and their pharmaceutically acceptable salts are prepared and disclosed as CCR5 antagonists. Thus, II was prepared by reaction of [3-(2,2-dimethylpropanoyl)-6-phenyl-1,3-oxazinan-6-yl]acetaldehyde (preparation given) with 1-[(1R,5S)-8-azabicyclo[3.2.1]oct-3-yl]-2-methyl-1H-benzimidazole dihydrochloride. I have pIC50 values of ≥5 in assays for CCR5 antagonism. As CCR5 antagonists, I are useful for the treatment of viral infections (particularly HIV infection).

IT **104227-87-4**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug for therapeutic administration; **preparation** of oxazine and morpholine derivs. as CCR5 antagonists)

RN 104227-87-4 CAPLUS

CN 1,3-Propanediol, 2-[2-(2-amino-9H-purin-9-yl)ethyl]-, diacetate (ester) (9CI) (CA INDEX NAME)



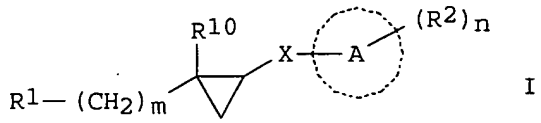
REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 12 OF 66 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:534198 CAPLUS
DOCUMENT NUMBER: 141:88871
TITLE: Preparation of aminoalkylaryl cyclopropyl compounds as CCR5 antagonists
INVENTOR(S): Peckham, Jennifer Poole; Aquino, Christopher Joseph; Kazmierski, Wieslaw Mieczyslaw
PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA
SOURCE: PCT Int. Appl., 138 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004055010	A2	20040701	WO 2003-US39619	20031212
WO 2004055010	A3	20041223		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2002-433626P P 20021213
OTHER SOURCE(S): MARPAT 141:88871
GI



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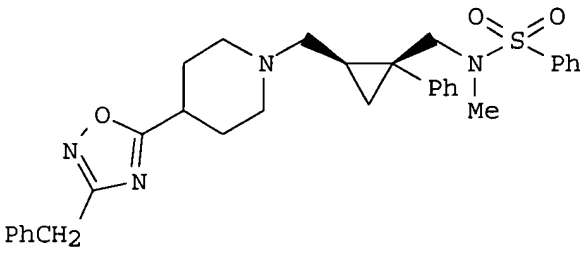


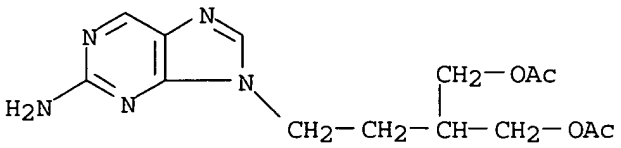
II

AB Title compds. I [R1 = (un)substituted saturated, partially saturated, or aromatic 4-7 monocyclic or 8-10 membered bicyclic ring having one ring nitrogen and 0-4 addnl. heteroatoms selected from O, P, S or N, optionally attached through alkylene chain, substituted-amine, -amide, etc.; R2 = OH, halogen (un)substituted-alkyl, -alkoxy, -aryl, -heteroaryl, -cycloalkyl, etc., optionally two adjacent R2s taken together form a fused, saturated, partially saturated or aromatic 5-6 membered ring having 0-3 heteroatoms selected from O, P, S, or N, or two geminal R2s optionally taken together from a spiro, saturated, partially saturated or aromatic 5-6 membered ring having 0-3 heteroatoms selected from O, P, S or N, said fused or spiro ring being optionally substituted; R10 = H, (un)substituted-alkyl, -alkenyl, -alkynyl, -cycloalkyl, -heterocyclyl, -heteroaryl, or aryl; X = (un)substituted-alkylene chain which optionally may have 0-3 heteroatoms selected from O, P, S or N; A = saturated, partially saturated, or aromatic 3-7 monocyclic or 8-10 membered bicyclic ring having one ring nitrogen and 0-4 addnl. heteroatoms selected from O, P, S or N ; m = 0-3, n = 0-5] and their pharmaceutically acceptable salts are prepared and disclosed as CCR5 antagonists. Thus, II was prepared by reaction of N-{[(1S,2R)-2-formyl-1-phenylcyclopropyl]methyl}-N-methylbenzenesulfonamide (preparation given) and 4-(3-benzyl-1,2,4-oxadiazol-5-yl)piperidine. Addnl. preparative examples utilizing combinatorial methods of synthesis are given. I have pIC50 values of ≥5 in assays for CCR5 antagonism. As CCR5 antagonists, I are useful for the treatment of viral infections (particularly HIV infection).

IT **104227-87-4**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug for therapeutic administration; **preparation** of aminoalkylaryl cyclopropane derivs. as CCR5 antagonists)

RN 104227-87-4 CAPLUS

CN 1,3-Propanediol, 2-[2-(2-amino-9H-purin-9-yl)ethyl]-, diacetate (ester) (9CI) (CA INDEX NAME)



L5 ANSWER 13 OF 66 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:531360 CAPLUS
DOCUMENT NUMBER: 141:88873
TITLE: Preparation of heterocyclylalkyl substituted cyclohexyl compounds as CCR5 antagonists
INVENTOR(S): Duan, Maosheng; Kazmierski, Wieslaw Mieczyslaw; Aquino, Christopher Joseph
PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA
SOURCE: PCT Int. Appl., 103 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004054581	A2	20040701	WO 2003-US39732	20031212
WO 2004054581	A3	20050203		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2002-433552P P 20021213
OTHER SOURCE(S): MARPAT 141:88873
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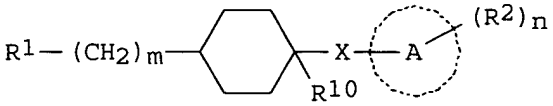

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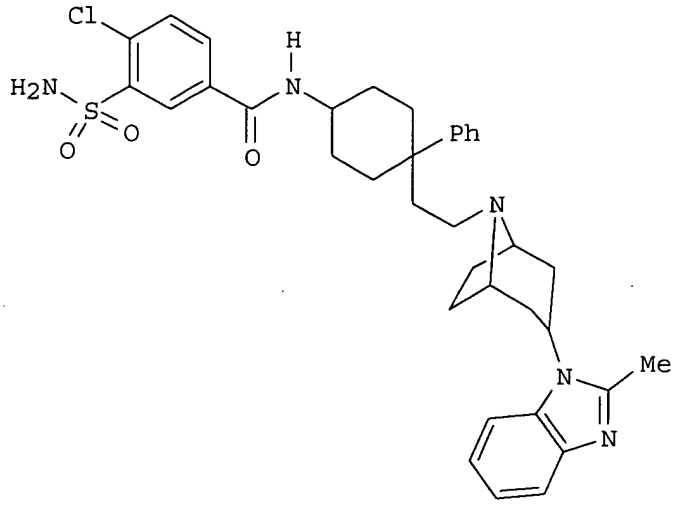


II

AB Title compds. I [R1 = (un)substituted saturated, partially saturated, or aromatic 4-7 monocyclic or 8-10 membered bicyclic ring having one ring nitrogen and 0-4 addnl. heteroatoms selected from O, P, S or N, optionally attached through alkylene chain, substituted-amine, -amide, etc.; R2 = OH, halogen (un)substituted-alkyl, -alkoxy, -aryl, -heteroaryl, -cycloalkyl, etc., optionally two adjacent R2s taken together form a fused, saturated, partially saturated or aromatic 5-6 membered ring having 0-3 heteroatoms selected from O, P, S, or N, or two geminal R2s optionally taken together from a spiro, saturated, partially saturated or aromatic 5-6 membered ring having 0-3 heteroatoms selected from O, P, S or N, said fused or spiro ring being optionally substituted; R10 = H, (un)substituted-alkyl, -alkenyl, -alkynyl, -cycloalkyl, -heterocyclyl, -heteroaryl, or aryl; X = (un)substituted-alkylene chain which optionally may have 0-3 heteroatoms selected from O, P, S or N; A = saturated, partially saturated, or aromatic 4-7 monocyclic or 8-10 membered bicyclic ring having one ring nitrogen and 0-4 addnl. heteroatoms selected from O, P, S or N ; m = 0 or 1, n = 0-5] and their pharmaceutically acceptable salts are prepared and disclosed as CCR5 antagonists. Thus, II was prepared by amidation of cis-4-{2-[3-(2-methyl-1H-benzimidazol-1-yl)-8-azabicyclo[3.2.1]oct-8-yl]ethyl}-4-phenylcyclohexanamine (preparation given) with 3-(aminosulfonyl)-4-chlorobenzoic acid. I have pIC50 values of ≥5 in assays for CCR5 antagonism. As CCR5 antagonists, I are useful for the treatment of viral infections (particularly HIV infection).

IT **104227-87-4**

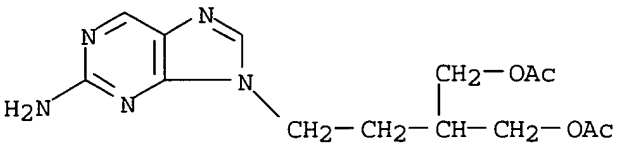
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (codrug for therapeutic administration; **preparation** of heterocyclylalkyl substituted cyclohexanes derivs. as CCR5 antagonists)

RN 104227-87-4 CAPLUS

CN 1,3-Propanediol, 2-[2-(2-amino-9H-purin-9-yl)ethyl]-, diacetate (ester)

Prepared by: Mary Hale @2-2507 Rem Bldg 1D86

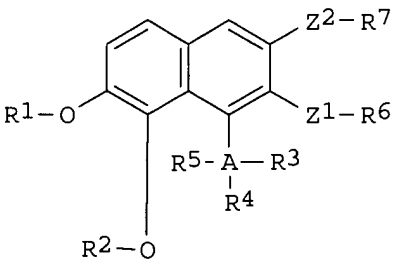
(9CI) (CA INDEX NAME)



L5 ANSWER 14 OF 66 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:182538 CAPLUS
DOCUMENT NUMBER: 140:235506
TITLE: Preparation of 1-arylnaphthalenes and related compounds as antiviral agents for the treatment of herpesviral infections
INVENTOR(S): Hsu, Tsu-an; Hsieh, Hsing-pang; Juan, Li-jung; Chang, Sui-yuan; Kuo, Yueh-hsiung
PATENT ASSIGNEE(S): Taiwan
SOURCE: U.S. Pat. Appl. Publ., 10 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2004044069	A1	20040304	US 2003-445268		20030523
PRIORITY APPLN. INFO.:			US 2002-382692P	P	20020523

OTHER SOURCE(S): MARPAT 140:235506
GI

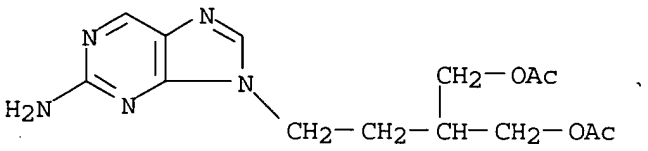


I

AB Title compds. I [R1, R2 = R, C(=O)R, R1 and R2 taken together is -(CH2)m-; R3, R4, R5 = R, OR, C(=O)R, etc.; A = aryl, e.g., phenyl; Z1, Z2 = CH2, C(=O); R6, R7 = R, OR, NRR', etc.; R, R' = H, alkyl, (CH2)p-aryl, etc.; m = 1-4, p = 0-6] were prepared For example, LAH reduction of lactone I [R1, R2 = -CH2-; Z2-R7-R6-Z1- = -CO2CH2-; A = Ph; R3-R4 = 3,4-(-OCH2O-), R5 = H] afforded diol I [R1, R2 = -CH2-; Z1-R6, Z2-R7 = CH2OH; A = Ph; R3-R4 = 3,4-(-OCH2O-), R5 = H] in 80% yield. In human herpesvirus 5 replication inhibition assays, the IC50 and LC50 values of compound I [R1, R2 = -CH2-; Z1-R7 = R6-Z2 = CH2OH; A = Ph; R3-R4 = 3,4-(-OCH2O-), R5 = H] were less than 0.1 μM and >16 μM, resp. Compds. I were claimed useful for the treatment of herpesvirus infections.

Prepared by: Mary Hale @2-2507 Rem Bldg 1D86

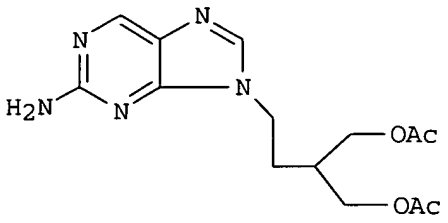
IT **104227-87-4, Famciclovir**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(medicaments with; **preparation** of 1-arylnaphthalenes and related compds. as antiviral agents for the treatment of herpesviral infections)
RN 104227-87-4 CAPLUS
CN 1,3-Propanediol, 2-[2-(2-amino-9H-purin-9-yl)ethyl]-, diacetate (ester) (9CI) (CA INDEX NAME)



L5 ANSWER 15 OF 66 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:60510 CAPLUS
DOCUMENT NUMBER: 140:111636
TITLE: Process for preparing 9-[4-acetoxy-3-(acetoxymethyl)but-1-yl]-2-aminopurine from 2-aminopurine and 2-acetoxymethyl-4-bromo-1-butyl acetate
INVENTOR(S): Lee, Byoung-Suk; Shin, Sang-Hoon
PATENT ASSIGNEE(S): Kyungdong Pharm. Co., Ltd., S. Korea
SOURCE: PCT Int. Appl., 17 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004007497	A1	20040122	WO 2003-KR1396	20030715
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1551839	A1	20050713	EP 2003-741578	20030715
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				

PRIORITY APPLN. INFO.: KR 2002-41267 A 20020715
WO 2003-KR1396 W 20030715
OTHER SOURCE(S): CASREACT 140:111636
GI



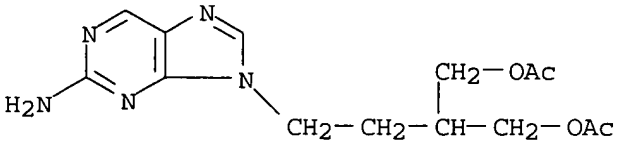
I

AB Disclosed is a process for **preparing** 9-[4-acetoxy-3-(acetoxymethyl)but-1-yl]-2-aminopurine [**Famciclovir** (I)], a drug of purine derivs. having antiviral activity. This process comprises reacting 2-aminopurine with 2-acetoxymethyl-4-bromo-1-Bu acetate in the presence of thallium(I) ethoxide to give the desired compound I. According to this process, the desired compound can be **prepared** in very high selectivity and purity under mild reaction conditions.

IT **104227-87-4P**, **Famciclovir**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**preparation** of **famciclovir** from 2-aminopurine and 2-acetoxymethyl-4-bromo-1-Bu acetate with thalium ethoxide)

RN 104227-87-4 CAPLUS

CN 1,3-Propanediol, 2-[2-(2-amino-9H-purin-9-yl)ethyl]-, diacetate (ester) (9CI) (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 16 OF 66 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:60442 CAPLUS

DOCUMENT NUMBER: 140:128052

TITLE: An improved process for the **preparation** of 2-acetoxymethyl-4-halo-but-1-yl acetates, useful as intermediates for the antiviral agents penciclovir and **famciclovir**, from 3-(hydroxymethyl)tetrahydrofuran via regioselective ring opening

INVENTOR(S): Saladino, Raffaele; Ciambecchini, Umberto; Mancinetti, Daniele; Bonifacio, Fausto; Crescenzi, Cristina

PATENT ASSIGNEE(S): Recordati S.A., Switz.

SOURCE: PCT Int. Appl., 23 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

Prepared by: Mary Hale @2-2507 Rem Bldg 1D86

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004007418	A1	20040122	WO 2003-EP7237	20030707

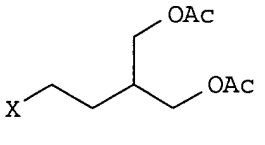
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

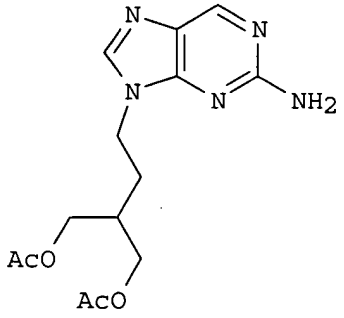
PRIORITY APPLN. INFO.: IT 2002-MI1533 A 20020712

OTHER SOURCE(S): MARPAT 140:128052

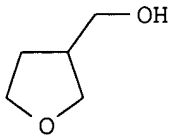
GI



I



II



III

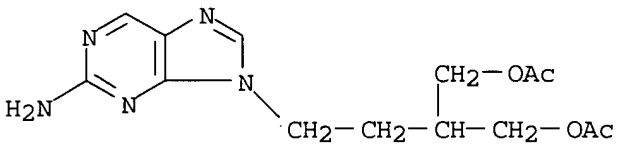
AB An improved, regioselective process for the **preparation** of 2-acetoxymethyl-4-halo-but-1-yl acetates [I; X = bromo or iodo] is disclosed. I are useful intermediates for the **preparation** of antiviral medicaments such as penciclovir and **famciclovir** (II). The method involves ring opening of 3-(hydroxymethyl)tetrahydrofuran (III) in the presence of an acylating agent and a Lewis acid selected from magnesium bromide and samarium triiodide. The method can involve a single step, or a 2-step process wherein the first step is O-acylation of III, and the second step is ring opening of the resultant III ester by the invention method. A variety of acyl chlorides and anhydrides may be used, provided that the acyl groups are eventually replaced by acetyl. The invention method does not give undesirable dihalide byproducts, and little or none of the isomeric 2-halomethyl-4-acetoxybut-1-yl acetate byproducts, both of which are difficult to sep. from I, and which can react with purines to give further byproducts, thereby decreasing yields of the final drugs. For example, a suspension of MgBr2 in MeCN at 0° was treated with Ac2O and then with III. The reaction was refluxed to completion (18 h) to show quant. conversion and 75% yield of a 90%/10% mixture of I [X = Br] and its isomer, namely 2-bromomethyl-4-acetoxybutyl 1-acetate. This impure product mixture was used directly in reaction with 2-amino-6-chloropurine (DMF, K2CO3, room temperature, 18 h), without formation of byproducts due to the minor isomer (this isomer can nevertheless be removed by fractional distillation if desired). Products due to N-alkylation by

I at the 9- and 7-positions of the purine nucleus were obtained in yields of 58% and 8%. The 9-isomeric alkylation product was dechlorinated with ammonium formate and Pd/C in refluxing MeOH to give II in 90% yield. A comparative experiment using NaI and AcCl in MeCN gave only 55% yield of I [X = iodo].

IT **104227-87-4P, Famciclovir**
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(antiviral agent; improved **preparation** of (acetoxymethyl)halobutyl acetates as intermediates for penciclovir and **famciclovir**, by acylation and Lewis acid-catalyzed ring opening of (hydroxymethyl)tetrahydrofuran)

RN 104227-87-4 CAPLUS

CN 1,3-Propanediol, 2-[2-(2-amino-9H-purin-9-yl)ethyl]-, diacetate (ester) (9CI) (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 17 OF 66 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:1007859 CAPLUS

DOCUMENT NUMBER: 140:59661

TITLE: Preparation of immunosuppressive poly-substituted pteridinediones (lumazines)

INVENTOR(S): Waer, Mark Jozef Albert; Herdewijn, Piet Andre Maurits Maria; Pfleiderer, Wolfgang Eugen

PATENT ASSIGNEE(S): Belg.

SOURCE: U.S. Pat. Appl. Publ., 47 pp., Cont.-in-part of U.S. Ser. No. 890,500, abandoned.
CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003236255	A1	20031225	US 2003-444158	20030523
WO 2000045800	A2	20000810	WO 2000-EP938	20000202
WO 2000045800	A3	20020110		

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1479682	A1	20041124	EP 2003-79183	20031224

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,

IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
WO 2004104005 A2 20041202 WO 2004-EP5501 20040521
WO 2004104005 A3 20050127
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
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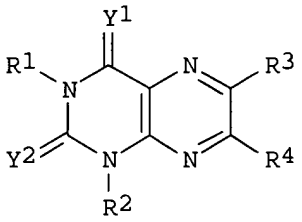
PRIORITY APPLN. INFO.: US 1999-118235P P 19990202
US 1999-118282P P 19990202
US 1999-118295P P 19990202
WO 2000-EP938 W 20000202
US 2001-890500 B2 20011030
US 2003-444158 A 20030523
EP 2003-79183 A 20031224
OTHER SOURCE(S): MARPAT 140:59661
GI



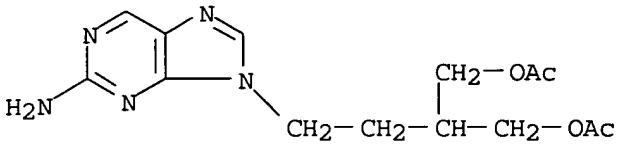
I

AB The title compds. [I; R1 = H, alkyl, aryl, alkylaryl, etc.; R2 = H, alkyl, aryl, alkylaryl, etc.; R3, R4 = H, F, I, alkyl, etc.; Y1, Y2 = O, S; with provisos], useful as biol. active ingredients in preparing pharmaceutical compns. especially for the treatment or prevention of a CNS disorder, a cell proliferative disorder, a viral infection, an immune or auto-immune disorder or a transplant rejection, were prepared Thus, treating 1,3-dimethyllumazin-6-triphenylphosphonomethyl bromide (preparation given) with NaOMe in MeOH followed addition of pyridine-3-carboxaldehyde afforded 66% 1,3-dimethyl-6-[(E)-2-(pyrid-3-yl)vinyl]lumazine which showed IC50 of 30 μM in the mixed lymphocyte reaction (MLR) test which is considered as in vitro analog of the transplant rejection in vivo test. Combinations of the pteridine derivs. I with an immunosuppressant or immunomodulator drug, an antineoplastic drug or an antiviral agent, providing potential synergistic effects, are also disclosed.

IT **104227-87-4**, **Famciclovir**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(co-administration; **preparation** of immunosuppressive pteridinediones for use in combination with antiviral agents)

RN 104227-87-4 CAPLUS

CN 1,3-Propanediol, 2-[2-(2-amino-9H-purin-9-yl)ethyl]-, diacetate (ester) (9CI) (CA INDEX NAME)



L5 ANSWER 18 OF 66 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:257320 CAPLUS
DOCUMENT NUMBER: 138:260488
TITLE: Method for the production of sterile liquid preparations for inhalation
INVENTOR(S): Keller, Manfred; Lintz, Frank
PATENT ASSIGNEE(S): Pari Gmbh, Germany
SOURCE: Ger. Offen., 14 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

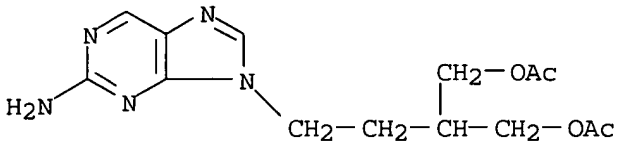
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 10145361	A1	20030403	DE 2001-10145361	20010914
EP 1417958	A1	20040512	EP 2002-25006	20021108
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
CA 2475577	AA	20040521	CA 2003-2475577	20031028
WO 2004041253	A1	20040521	WO 2003-EP11949	20031028
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1558217	A1	20050803	EP 2003-772269	20031028
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				

PRIORITY APPLN. INFO.:
DE 2001-10145361 A 20010914
EP 2002-25006 A 20021108
WO 2003-EP11949 W 20031028

AB The invention concerns the production of sterile aqueous inhalation aerosols containing slightly soluble drugs by (a) preparing an aqueous suspension containing drug particles larger than 1 μm and a dissolved surfactant; (b) reduction of the particle size by high pressure homogenization or collision jet grinding to obtain particles less than 1 μm; (c) heat treatment of the suspension for sterilization, the final average particle size is less than 2 μm. The inhalants are formulated for pulmonary and nasal use. Suspensions can be nebulized by aerosol nozzles, ultrasound, vibrating membranes with defined pore sizes or electrohydrodynamically.

IT **104227-87-4, Famciclovir**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method for production of sterile liquid **prepns.** for inhalation)

RN 104227-87-4 CAPLUS
CN 1,3-Propanediol, 2-[2-(2-amino-9H-purin-9-yl)ethyl]-, diacetate (ester) (9CI) (CA INDEX NAME)



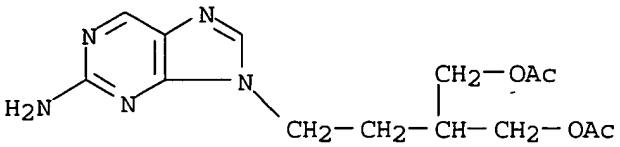
L5 ANSWER 19 OF 66 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:172973 CAPLUS
DOCUMENT NUMBER: 138:205303
TITLE: Production method of **famciclovir** and production and **crystallization** method of intermediate therefor
INVENTOR(S): Hijiya, Toyoto; Torii, Takayoshi; Izawa, Kunisuke
PATENT ASSIGNEE(S): Ajinomoto Co., Inc., Japan
SOURCE: Eur. Pat. Appl., 10 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1288215	A1	20030305	EP 2002-19301	20020828
EP 1288215	B1	20041215		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
JP 2003146988	A2	20030521	JP 2002-245709	20020826
US 2003056712	A1	20030327	US 2002-231249	20020830
US 6761767	B2	20040713		

PRIORITY APPLN. INFO.: JP 2001-262301 A 20010830
OTHER SOURCE(S): CASREACT 138:205303; MARPAT 138:205303
AB An N-9-position alkylated form is selectively precipitated by subjecting a mixture containing the N-9-position alkylated form and an N-7-position alkylated form of 2-amino-6-halopurine to a **crystallization** step using a mixed solvent of an organic solvent and water. Then, this N-9-position alkylated form is reduced to give **famciclovir.** By this method of the present invention, **famciclovir** known as an antiviral agent, and an intermediate compound therefor can be efficiently produced. Thus, coupling of 2-acetoxymethyl-4-methanesulfonoxy-1-Bu acetate with 2-amino-6-chloropurine gave 64 % yield of 2-acetoxymethyl-4-(2-amino-6-chloropurin-9-yl)-1-Bu acetate, which was converted to **famciclovir**.

IT **104227-87-4P**
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(production method and **crystallization** of **famciclovir** via coupling of 2-acetoxymethyl-4-methanesulfonoxy-1-Bu acetate with 2-amino-6-chloropurine)
RN 104227-87-4 CAPLUS
CN 1,3-Propanediol, 2-[2-(2-amino-9H-purin-9-yl)ethyl]-, diacetate (ester)

(9CI) (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

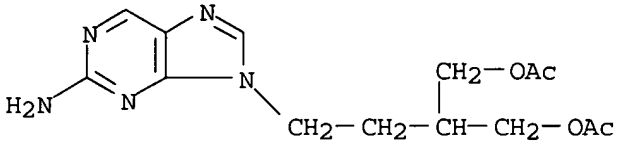
L5 ANSWER 20 OF 66 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:66403 CAPLUS
DOCUMENT NUMBER: 138:394835
TITLE: Synthesis and stereochemical characterisation of platinum(II) complexes with the antiviral agents penciclovir and famciclovir
AUTHOR(S): Cerasino, Leonardo; Intini, Francesco P.; Kobe, Joze; de Clercq, Erik; Natile, Giovanni
CORPORATE SOURCE: Dipartimento Farmaco-Chimico, Universita degli Studi di Bari, Bari, I-70125, Italy
SOURCE: Inorganica Chimica Acta (2003), 344, 174-182
CODEN: ICHAA3; ISSN: 0020-1693
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 138:394835

AB The synthesis and the stereochem. characterization of Pt complexes containing one mol. of antiviral drug, penciclovir or famciclovir (L), and different sets of ancillary ligands (Clx(NH3)3-x, x = 1 or 2, and N,N,N',N'',N''-pentamethyldiethylenetriamine, pmdien) are reported. Penciclovir is a guanosine analog, while famciclovir is a prodrug of penciclovir lacking the O in position 6 of the purine ring. The study has allowed comparison of structural features of Pt derivs. with different bulk of the carrier ligand(s) and of the purines. NMR expts. (particularly diagnostic are the H8 and H6 chemical shifts of the purine) indicate that in compds. with non bulky carrier ligands (Clx(NH3)3-x) the purine is free to rotate about the Pt-N7 bond. In contrast, in complexes with bulky carrier ligand (pmdien) there is restricted rotation about the Pt-N7 bond and the purine is constrained in a quasi orthogonal position with respect to the Pt coordination plane. Because of the slow rotation for [Pt(pmdien)(L)]2+ two rotamers are observed in solution differing for the relative positions of the six-membered ring of the purine and the central N-Me of pmdien with respect to the Pt coordination plane (on the same side or on opposite sides for endo and exo rotamers, resp.). Penciclovir, having an O atom in position 6 of the purine ring, favors the exo over the endo rotamer while famciclovir, having just a H atom in position 6, favors the endo over the exo rotamer. The change in rotamer preference suggests that intramol. interactions involving mostly the substituent in position 6 of the purine and the terminal N-methyls of pmdien have opposite character for the two antiviral ligands. Biol. tests confirmed that cationic Pt species cis-[PtCl(NH3)2(L)]+ can have cytotoxicity towards tumor cells greater than corresponding compds. cis-[PtCl2(NH3)(L)].

IT **104227-87-4, Famciclovir**
RL: RCT (Reactant); RACT (Reactant or reagent)
(for **preparation** of platinum(II) pentamethyldiethylenetriamine complexes with the antiviral agents penciclovir/**famciclovir**)

Prepared by: Mary Hale @2-2507 Rem Bldg 1D86

RN 104227-87-4 CAPLUS
CN 1,3-Propanediol, 2-[2-(2-amino-9H-purin-9-yl)ethyl]-, diacetate (ester) (9CI) (CA INDEX NAME)



REFERENCE COUNT: 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 21 OF 66 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:5729 CAPLUS
DOCUMENT NUMBER: 138:56191
TITLE: Preparation, antiviral activity, and cytotoxicity of β-2'- and 3'-halo-nucleosides
INVENTOR(S): Chu, Chung K.; Otto, Michael J.; Shi, Junxing; Schinazi, Raymond F.; Choi, Yongseok; Gumina, Giuseppe; Chong, Youhoon; et al.
PATENT ASSIGNEE(S): Pharmasset Ltd., Barbados; University of Georgia Research Foundation, Inc.; Emory University
SOURCE: PCT Int. Appl., 220 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2003000200	A2	20030103	WO 2002-US20245		20020624
WO 2003000200	A3	20040902			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW					
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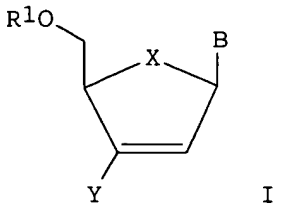
CA 2451745	AA	20030103	CA 2002-2451745		20020624
EP 1478322	A2	20041124	EP 2002-756310		20020624
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR					
JP 2005503358	T2	20050203	JP 2003-506646		20020624
US 2005119286	A1	20050602	US 2002-179612		20020624
PRIORITY APPLN. INFO.:			US 2001-300356P	P	20010622
			US 2001-305386P	P	20010713
			WO 2002-US20245	W	20020624

OTHER SOURCE(S): MARPAT 138:56191
GI



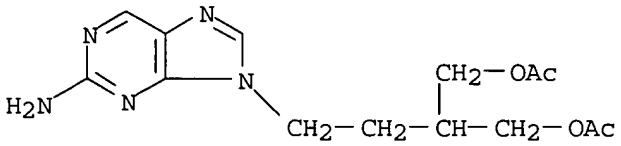
I

AB The present invention includes compds. and compns. of β-halo-nucleosides I wherein: R1 is hydrogen, straight chained, branched or cyclic alkyl, CO-alkyl, CO-aryl, CO- alkoxyalkyl, CO-aryloxyalkyl, CO-substituted aryl, alkylsulfonyl, arylsulfonyl, aralkylsulfonyl, amino acid residue, mono, di, or triphosphate, or a phosphate derivative; X is O, S, SO2 or CH2; Y is fluoro, chloro, bromo or iodo; and B is a purine or pyrimidine base that may optionally be substituted, as well as methods to treat HIV, HBV or abnormal cellular proliferation comprising administering said compds. or compns. Thus, (-)-1-[(1S,4R)-2,3-dideoxy-2,3-didehydro-2-fluoro-4-thio-β-D-ribofuranosyl]-cytosine was prepared and tested in vitro as antiviral agent. Preferred examples of antiviral agents can be used in combination or alternation with other known antiviral agents for HIV therapy. Use of the any one of the pharmaceutical compns. for the treatment and/or prophylaxis of an HIV infection or an abnormal cellular proliferation in a host.

IT **104227-87-4, Famciclovir**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**preparation**, antiviral activity, and cytotoxicity of β-2'- and 3'-halo-nucleosides)

RN 104227-87-4 CAPLUS

CN 1,3-Propanediol, 2-[2-(2-amino-9H-purin-9-yl)ethyl]-, diacetate (ester) (9CI) (CA INDEX NAME)



L5 ANSWER 22 OF 66 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:905731 CAPLUS

DOCUMENT NUMBER: 138:14152

TITLE: Preparation of enzymic ribonucleic acid peptide conjugates as antitumor and antiviral agents and compositions for cellular delivery

INVENTOR(S): Beigelman, Leonid; Matulic-Adamic, Jasenka; Vargeese, Chandra; Karpeisky, Alexander; Blatt, Lawrence; Shaffer, Christopher

PATENT ASSIGNEE(S): Ribozyme Pharmaceuticals, Inc, USA

SOURCE: PCT Int. Appl., 220 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

Prepared by: Mary Hale @2-2507 Rem Bldg 1D86

FAMILY ACC. NUM. COUNT: 187
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002094185	A2	20021128	WO 2002-US15876	20020520
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 9851819	A1	19980611	AU 1998-51819	19980112
AU 729657	B2	20010208		
AU 9939188	A1	19990916	AU 1999-39188	19990713
AU 769175	B2	20040115	AU 2000-56616	20000911
US 2003104985	A1	20030605	US 2002-151116	20020517
CA 2447161	AA	20021128	CA 2002-2447161	20020520
JP 2005505504	T2	20050224	JP 2002-590906	20020520
US 2003130186	A1	20030710	US 2002-201394	20020722
US 2004110296	A1	20040610	US 2003-427160	20030430
US 2004192626	A1	20040930	US 2003-444853	20030523
US 2005080031	A1	20050414	US 2003-724270	20031126
US 2005020525	A1	20050127	US 2004-757803	20040114
US 2004249178	A1	20041209	US 2004-780447	20040213
US 2005096284	A1	20050505	US 2004-783128	20040220
US 2005014172	A1	20050120	US 2004-798090	20040311
US 2005048529	A1	20050303	US 2004-800487	20040315
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US 2005054598	A1	20050310	US 2004-830569	20040423
US 2005148530	A1	20050707	US 2004-831620	20040423
US 2005137153	A1	20050623	US 2004-840731	20040506
US 2005171039	A1	20050804	US 2004-844076	20040511
US 2005159376	A1	20050721	US 2004-844072	20040512
US 2005137155	A1	20050623	US 2004-861060	20040603
US 2005143333	A1	20050630	US 2004-863973	20040609
US 2005171040	A1	20050804	US 2004-864044	20040609
US 2005119211	A1	20050602	US 2004-869638	20040616
US 2005119212	A1	20050602	US 2004-871222	20040618
US 2005124566	A1	20050609	US 2004-879867	20040628
US 2005130181	A1	20050616	US 2004-881118	20040630
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US 2005124568	A1	20050609	US 2004-888226	20040709
US 2005124569	A1	20050609	US 2004-892922	20040716
US 2005164224	A1	20050728	US 2004-893010	20040716
US 2005070497	A1	20050331	US 2004-894475	20040719
US 2005159378	A1	20050721	US 2004-915896	20040811
US 2005159379	A1	20050721	US 2004-916030	20040811
US 2005158735	A1	20050721	US 2004-916095	20040811
US 2005153914	A1	20050714	US 2004-918969	20040816
US 2005164966	A1	20050728	US 2004-918896	20040816
US 2005136436	A1	20050623	US 2004-923640	20040819
US 2005153915	A1	20050714	US 2004-922544	20040819
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US 2005159382	A1	20050721	US 2004-923580	20040819

US 2005164967	A1	20050728	US 2004-922034		20040819
US 2005079610	A1	20050414	US 2004-923115		20040820
US 2005153916	A1	20050714	US 2004-923330		20040820
US 2005159381	A1	20050721	US 2004-923522		20040820
US 2005164968	A1	20050728	US 2004-923329		20040820
US 2005170371	A1	20050804	US 2004-922340		20040820
PRIORITY APPLN. INFO.:			US 2001-292217P	P	20010518
			US 2001-306883P	P	20010720
			US 2001-311865P	P	20010813
			US 2002-362016P	P	20020306
			AU 1995-26422	A3	19950518
			US 1996-623891	A	19960325
			AU 1996-76662	A3	19961025
			US 2001-294140P	P	20010529
			US 2001-296249P	P	20010606
			US 2001-318471P	P	20010910
			US 2002-358580P	P	20020220
			US 2002-363124P	P	20020311
			US 2002-374722P	P	20020422
			WO 2002-US15876	W	20020520
			US 2002-157580	A2	20020529
			WO 2002-US16840	A2	20020529
			WO 2002-US17674	A2	20020529
			US 2002-163552	A2	20020606
			US 2002-386782P	P	20020606
			US 2002-393796P	P	20020703
			US 2002-396600P	P	20020717
			US 2002-206705	A2	20020726
			US 2002-399348P	P	20020729
			US 2002-404039P	P	20020815
			US 2002-225023	A2	20020821
			US 2002-406784P	P	20020829
			US 2002-408378P	P	20020905
			US 2002-409293P	P	20020909
			US 2002-238700	A2	20020910
			US 2002-409785P	P	20020911
			US 2002-411275P	P	20020917
			US 2002-413714P	P	20020926
			US 2002-418655P	P	20021015
			US 2002-427467P	P	20021119
			US 2002-431105P	P	20021205
			US 2003-439922P	P	20030114
			US 2003-440129P	P	20030115
			WO 2003-US3662	A2	20030206
			WO 2003-US4088	A2	20030211
			WO 2003-US4123	A2	20030211
			WO 2003-US4566	A2	20030211
			WO 2003-US4250	A2	20030213
			WO 2003-US4397	A2	20030213
			WO 2003-US4402	A2	20030213
			WO 2003-US4738	A2	20030218
			WO 2003-US4907	A2	20030218
			WO 2003-US5022	A2	20030220
			WO 2003-US5028	A2	20030220
			WO 2003-US5044	A2	20030220
			WO 2003-US5162	A2	20030220
			WO 2003-US5190	A	20030220
			WO 2003-US5234	A2	20030220
			WO 2003-US5326	A2	20030220

WO 2003-US5346	A2	20030220
US 2003-417012	A1	20030416
US 2003-420194	A2	20030422
WO 2003-US12626	A2	20030422
US 2003-422704	A2	20030424
US 2003-427160	A2	20030430
US 2003-444853	A2	20030523
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US 2003-652791	A2	20030829
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US 2004-543480P	P	20040210
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US 2004-826966	A2	20040416
WO 2004-US11848	A2	20040416
US 2004-831620	A2	20040423
WO 2004-US13456	A2	20040430
US 2004-844072	A2	20040512
WO 2004-US16390	A2	20040524

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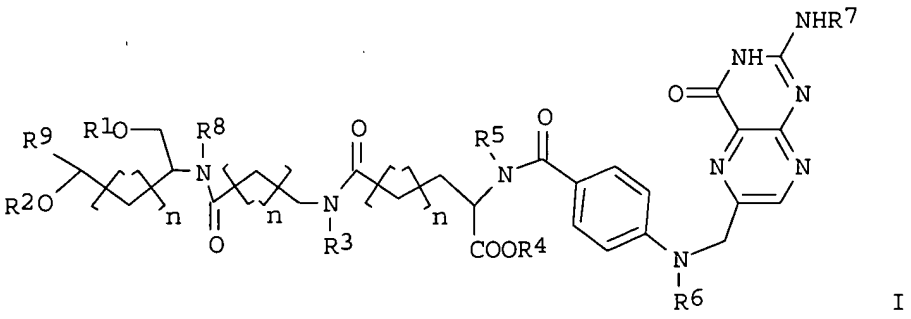


I

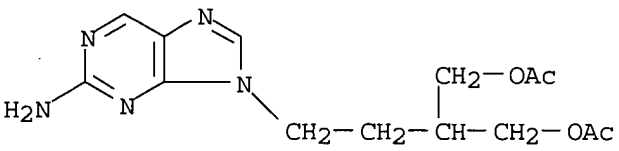
AB This invention features peptide nucleotide conjugates I wherein each R1-R8 are independently hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, or a protecting group, each "n" is independently an integer from 0 to about 200, R9 is a straight or branched chain alkyl, substituted alkyl, aryl, or substituted aryl, and R2 is a phosphorus containing group, nucleoside, nucleotide, small mol., nucleic acid, or a solid support comprising a linker., degradable linkers, compns., methods of synthesis, and applications thereof, including folate, galactose, galactosamine, N-acetyl galactosamine, PEG, phospholipid, peptide and human serum albumin (HAS) derived conjugates of biol. active compds., including antibodies, antivirals, chemotherapeutics, peptides, proteins, hormones nucleosides,

nucleotides, non-nucleosides, and nucleic acids including enzymic nucleic acids, DNAzymes, allozymes, antisense, dsRNA, siRNA, triplex oligonucleotides, 2,5-A chimeras, decoys and aptamers. Thus, 1-O-(4-monomethoxytrityl)-N-(12'-hydroxydodecanoyl-2-acetamido-3,4,6-tri-O-acetyl-2-deoxy-3-D-galactopyranose)-D-threoninol 3-O-(2-cyanoethyl,N,N-diisopropylphosphorami-dite) was prepared and incorporated into RNA. A method of treating a cancer patient, comprising contacting cells of patient wherein said cancer is breast cancer, lung cancer, colorectal cancer, brain cancer, esophageal cancer, stomach cancer, bladder cancer, pancreatic cancer, cervical cancer, head and neck cancer, ovarian cancer, melanoma, lymphoma, glioma, or multidrug resistant cancers and/or viral infections including HIV, HBV, HCV, CMV, RSV, HSV, poliovirus, influenza, rhinovirus, west nile virus, Ebola virus, foot and mouth virus, and papilloma.

IT **104227-87-4, Famciclovir**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**preparation** of enzymic RNA peptide conjugates as antitumor and antiviral agents and compns. for cellular delivery)

RN 104227-87-4 CAPLUS

CN 1,3-Propanediol, 2-[2-(2-amino-9H-purin-9-yl)ethyl]-, diacetate (ester) (9CI) (CA INDEX NAME)



L5 ANSWER 23 OF 66 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:695941 CAPLUS
DOCUMENT NUMBER: 137:232453
TITLE: Preparation of substituted benzophenones as inhibitors of reverse transcriptase
INVENTOR(S): Chan, Joseph Howing
PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA
SOURCE: PCT Int. Appl., 163 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002070470	A2	20020912	WO 2002-US6037	20020228
WO 2002070470	A3	20030306		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2439820	AA	20020912	CA 2002-2439820		20020228
EP 1363877	A2	20031126	EP 2002-723265		20020228
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
BR 2002007752	A	20040323	BR 2002-7752		20020228
CN 1494528	A	20040505	CN 2002-805882		20020228
NZ 527864	A	20040528	NZ 2002-527864		20020228
JP 2004525914	T2	20040826	JP 2002-569791		20020228
ZA 2003006549	A	20041122	ZA 2003-6549		20030821
NO 2003003857	A	20031027	NO 2003-3857		20030901
US 2004122064	A1	20040624	US 2004-469104		20040205
PRIORITY APPLN. INFO.:			US 2001-272953P	P	20010302
			WO 2002-US6037	W	20020228

OTHER SOURCE(S): MARPAT 137:232453
GI

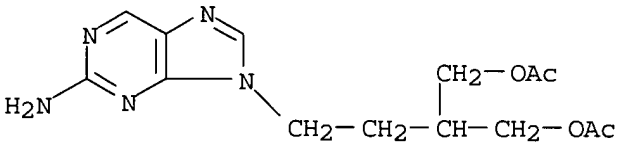
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [R1 = ≥1 substituent chosen from halo, CF3, alkyl, aminoalkyl, alkoxy, CN, NO2, NH2, thioalkoxy, etc.; R2 = H, halo, alkyl, NO2, NH2, alkylamino, CF3, alkoxy; R3 = OH, halo, CF3, NO2, alkyl; R4 = sulfonamido, sulfonylimino, etc.;] were prepared For instance, 3,5-dichlorobromobenzene was metalated (MTBE, n-BuLi, -50°) and acylated with the N,2-dimethoxy-N-methyl-5-chlorobenzamide and the resulting benzophenone converted to II. II was converted to III in 5 steps. Polymorphic forms of sodium, choline, calcium, magnesium, ethanolamine and triethylamine salts of III were prepared and characterized. Oral bioavailability and solubility parameters were determined for III and polymorphic salt forms thereof. Compds. of the present invention have anti-HIV activity and deliver compds. that have anti- HIV activity in the range IC50 = 1-1000 nM against wild type and mutant viruses.

IT **104227-87-4**, **Famciclovir**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination pharmaceutical; **preparation** of substituted benzophenones as inhibitors of reverse transcriptase)

RN 104227-87-4 CAPLUS

CN 1,3-Propanediol, 2-[2-(2-amino-9H-purin-9-yl)ethyl]-, diacetate (ester) (9CI) (CA INDEX NAME)



L5 ANSWER 24 OF 66 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:	2002:669670 CAPLUS
DOCUMENT NUMBER:	137:185764
TITLE:	Preparation of amino acid-containing β-L-2'-deoxy-nucleosides as antiviral agents for the treatment of hepatitis B
INVENTOR(S):	Gosselin, Gilles; Imbach, Jean-louis; Bryant, Martin L.

Prepared by: Mary Hale @2-2507 Rem Bldg 1D86

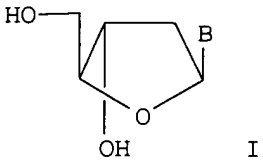
PATENT ASSIGNEE(S): Novirio Pharmaceuticals Limited, Cyprus; Centre National De La Recherche Scientifique
SOURCE: U.S., 31 pp., Cont.-in-part of U.S. 6,395,716.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6444652	B1	20020903	US 1999-459150	19991210
US 6395716	B1	20020528	US 1999-371747	19990810
EP 1431304	A2	20040623	EP 2004-75926	19990810
EP 1431304	A3	20050525		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
US 6566344	B1	20030520	US 2001-22148	20011214
US 6569837	B1	20030527	US 2001-22276	20011214
US 2003220290	A1	20031127	US 2003-437802	20030513
US 2003225028	A1	20031204	US 2003-438167	20030513

PRIORITY APPLN. INFO.:

US 1998-96110P	P	19980810
US 1999-131352P	P	19990428
US 1999-371747	A2	19990810
EP 1999-941027	A3	19990810
US 1999-459150	A1	19991210
US 2001-22148	A1	20011214
US 2001-22276	A1	20011214

OTHER SOURCE(S): MARPAT 137:185764
GI

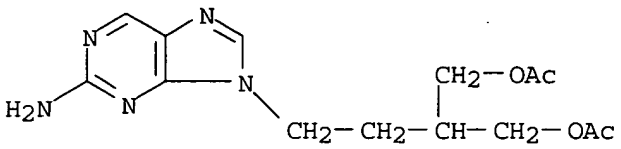


I

AB This invention is directed to a method for treating a host infected with hepatitis B comprising administering an effective amount of an anti-HBV biol. active 2'-deoxy-β-L-erythro-pentofuranonucleoside or a pharmaceutically acceptable salt or prodrug thereof, wherein the 2'-deoxy-β-L-erythro-pentofuranonucleoside has the formula I: wherein R is selected from the group consisting of H, straight chained, branched or cyclic alkyl, CO-alkyl, CO-aryl, CO-alkoxyalkyl, CO-aryloxyalkyl, CO-substituted aryl, alkylsulfonyl, arylsulfonyl, aralkylsulfonyl, amino acid residue, mono, di, or triphosphate, or a phosphate derivative; and B is a purine or pyrimidine base which may be optionally substituted. The 2'-deoxy-β-L-erythro-pentofuranonucleoside or a pharmaceutically acceptable salt or prodrug thereof may be administered either alone or in combination with another 2'-deoxy-β-L-erythro-pentofuranonucleoside or in combination with another anti-hepatitis B agent. Thus, 2'-deoxy-β-L-cytidine (β-L-dC) was prepared as antiviral agents for the treatment of hepatitis B. The inhibition of hepatitis B replication in 2.2.15 cells by β-L-dA and β-L-dC, alone and in combination was measured (EC50 = 0.0005-0.5 μM).

Prepared by: Mary Hale @2-2507 Rem Bldg 1D86

IT **104227-87-4, Famciclovir**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**preparation** of β-L-2'-deoxy-nucleosides as antiviral agents for the treatment of hepatitis B)
RN 104227-87-4 CAPLUS
CN 1,3-Propanediol, 2-[2-(2-amino-9H-purin-9-yl)ethyl]-, diacetate (ester) (9CI) (CA INDEX NAME)



REFERENCE COUNT: 73 THERE ARE 73 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 25 OF 66 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:438053 CAPLUS
DOCUMENT NUMBER: 136:193423
TITLE: Genvir Flamel Technologies
AUTHOR(S): Barnard, Dale L.
CORPORATE SOURCE: Institute for Antiviral Research, Utah State University, Logan, UT, 84322-5600, USA
SOURCE: Current Opinion in Investigational Drugs (PharmaPress Ltd.) (2001), 2(5), 622-623
CODEN: COIDAZ
PUBLISHER: PharmaPress Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review is given. Flamel Technologies is developing Genvir (formerly known as Viropump), a twice-daily controlled-release formulation of aciclovir, for potential use in the treatment of herpes simplex virus and varicella zoster virus infections. Genvir utilizes Flamel's proprietary Micropump technol., a microparticle-based drug delivery system designed to extend the time of absorption of drugs in the small intestine. The drug shows a comparable therapeutic efficacy to valaciclovir and **famciclovir** (both GlaxoSmithKline) [313393]. Phase III trials were completed [302829]. In August 2000, Flamel field for regulatory approval for the treatment of herpes in France, as a prelude to a pan-European approval [378641] and is **preparing** an IND application to begin clin. trials for genital herpes in the US [245970].
REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 26 OF 66 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:128928 CAPLUS
DOCUMENT NUMBER: 134:281063
TITLE: Regioselective alkylation of guanines using 2-acetoxytetrahydrofurans
AUTHOR(S): Geen, G. R.; Kincey, P. M.; Spoors, P. G.
CORPORATE SOURCE: New Frontiers Science Park, SmithKline Beecham Pharmaceuticals, Harlow, Essex, CM19 5AW, UK
SOURCE: Tetrahedron Letters (2001), 42(9), 1781-1784
CODEN: TELEAY; ISSN: 0040-4039
PUBLISHER: Elsevier Science Ltd.

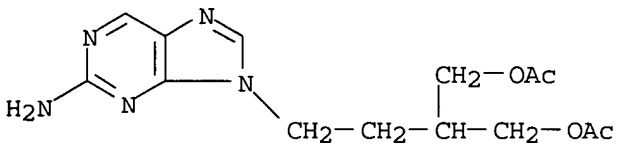
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 134:281063

AB Reaction of silylated guanine derivs. with 2-acetoxy-4-benzoyloxymethyltetrahydrofuran in DMF or NMP resulted in selective N-9 alkylation. This was used as the basis for a regioselective synthesis of the anti-viral agents famciclovir and penciclovir.

IT **104227-87-4P, Famciclovir**
RL: PNU (Preparation, unclassified); PREP (Preparation)
(**preparation** of **famciclovir** and penciclovir using a regioselective alkylation of silylguanines with 2-acetoxytetrahydrofurans)

RN 104227-87-4 CAPLUS

CN 1,3-Propanediol, 2-[2-(2-amino-9H-purin-9-yl)ethyl]-, diacetate (ester) (9CI) (CA INDEX NAME)



REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 27 OF 66 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:41285 CAPLUS
DOCUMENT NUMBER: 135:116203
TITLE: Current recommendations for the treatment of genital herpes
AUTHOR(S): Leung, Daniel T.; Sacks, Stephen L.
CORPORATE SOURCE: Wake Forest University School of Medicine, Winston Salem, NC, USA
SOURCE: Drugs (2000), 60(6), 1329-1352
CODEN: DRUGAY; ISSN: 0012-6667
PUBLISHER: Adis International Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 228 refs. The incidence of genital herpes continues to increase in epidemic-like fashion. Aciclovir (acyclovir) has been the original gold standard of therapy. The recent addition of **famciclovir** and valaciclovir as antiherpes drugs has improved convenience as well as the efficacy of treatment. Although aciclovir remains a widely prescribed and reliable drug, its administration schedule falls short of the ease of usage that the newer nucleoside analogs offer, for both episodic and suppressive therapy. Suppression of symptomatic disease and asymptomatic shedding from the genitalia have both become popular approaches, if not the primary targets of antiviral therapy. Knowing that asymptomatic disease leads to most cases of transmission strongly suggests that suppression with antiviral agents could reduce transmission risk in discordant couples. Unfortunately, the role for antivirals in reducing transmission remains to be proven in clin. trials. Neonatal herpes is now successfully treated using aciclovir. Current randomized clin. trials are examining aciclovir and valaciclovir administration, as well as safety and efficacy for post-acute suppressive therapy. Prevention of recurrences in pregnancy is also a topic under investigation, with a view to reducing the medical need for Cesarean section, or alternatively (and far less likely

to be accomplished) to protect the neonate. Although resistance is largely limited to the immunocompromised and a change in resistance patterns is not expected, several drugs are available for the treatment of aciclovir-resistant strains of herpes simplex. Foscarnet is the main alternative with proven efficacy in this setting. Unfortunately, administration of foscarnet requires i.v. therapy, although a single anecdote of topical foscarnet efficacy in this setting has been published. Alternatives include cidofovir gel, which is not com. available but can be formulated locally from the i.v. **preparation** Less effective alternatives include trifluridine and interferon. Future possibilities for treatment of genital herpes include a microparticle-based controlled-release formulation of aciclovir and resiquimod (VML-600; R-848). The search for an effective therapeutic vaccine for genital herpes has not been successful to date, although a live virus glycoprotein H-deficient (DISC) vaccine is currently in clin. trials. Recent data suggest that seroneg. women are protected (albeit, not fully) by a glycoprotein D recombinant vaccine with adjuvant. Despite the established safety and convenience of current treatment options, better suppressive options and topical treatment options are much needed. Studies using existing agents as potential tools to avoid Cesarean section, or transmission to neonate or partner are ongoing. Both vaccines and antivirals may eventually play a role in prevention of infection.

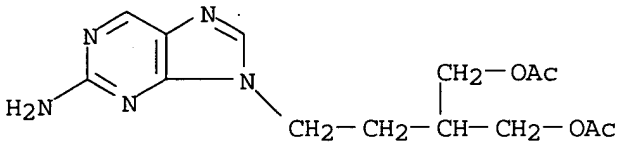
REFERENCE COUNT: 228 THERE ARE 228 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 28 OF 66 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:458477 CAPLUS
DOCUMENT NUMBER: 133:222945
TITLE: A new route to famciclovir via palladium catalyzed allylation
AUTHOR(S): Freer, Richard; Geen, Graham R.; Ramsay, Thomas W.; Share, Andrew C.; Slater, Graham R.; Smith, Neil M.
CORPORATE SOURCE: SmithKline Beecham Pharmaceuticals, New Frontiers Science Park, Essex, CM19 5AW, UK
SOURCE: Tetrahedron (2000), 56(26), 4589-4595
CODEN: TETRAB; ISSN: 0040-4020
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 133:222945

AB An efficient route to the acyclic nucleoside analog famciclovir has been developed based on a palladium(0) catalyzed coupling of 2-amino-6-chloropurine and an allylic carbonate side-chain derived from 2,2-dimethyl-1,3-dioxan-5-one. The reaction proceeds via a highly N-9 regioselective purine allylation step involving a novel palladium mediated N-7 to N-9 rearrangement.

IT **104227-87-4P, Famciclovir**
RL: SPN (Synthetic preparation); PREP (Preparation)
(**preparation** of **famciclovir** via palladium catalyzed allylation)

RN 104227-87-4 CAPLUS
CN 1,3-Propanediol, 2-[2-(2-amino-9H-purin-9-yl)ethyl]-, diacetate (ester) (9CI) (CA INDEX NAME)



REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 29 OF 66 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:171276 CAPLUS
DOCUMENT NUMBER: 132:207828
TITLE: Synthesis of a new antiviral medicine famciclovir
AUTHOR(S): Wang, En-si; Zhang, Guang-liang; Jin, Lei
CORPORATE SOURCE: College of Life Science, Jilin University, Changchun, 130023, Peop. Rep. China
SOURCE: Jilin Daxue Ziran Kexue Xuebao (2000), (1), 95-98
CODEN: CLTTDI; ISSN: 0529-0279
PUBLISHER: Jilin Daxue Ziran Kexue Xuebao Bianjibu
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
AB The title compound was prepared with 21 % yield via regioselective alkylation of 2-aminopurine with 5-(2-bromoethyl)-2,2-dimethyl-1,3-dioxan as a pivotal step. The route without highly toxic reagents and high presure and temperature may be applied to industrial production

ordered 8/22

L5 ANSWER 30 OF 66 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:98557 CAPLUS
DOCUMENT NUMBER: 132:137208
TITLE: Preparation of antiviral alkyl substituted purine derivatives
INVENTOR(S): Kobe, Joze; Jaksa, Suzana; Kalayanov, Genadij
PATENT ASSIGNEE(S): Kemijski Institut, Slovenia
SOURCE: PCT Int. Appl., 32 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2000006573	A1	20000210	WO 1999-SI21		19990728
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
SI 20022	C	20000229	SI 1998-216		19980729
AU 9948175	A1	20000221	AU 1999-48175		19990728
PRIORITY APPLN. INFO.:			SI 1998-216	A	19980729
			WO 1999-SI21	W	19990728

OTHER SOURCE(S): CASREACT 132:137208; MARPAT 132:137208

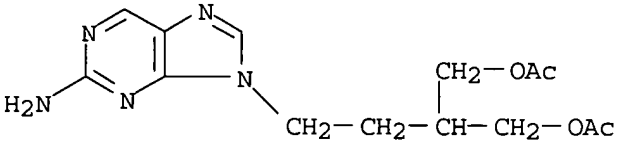
Prepared by: Mary Hale @2-2507 Rem Bldg 1D86

AB A new process for the preparation of alkyl substituted purine derivs., especially of N7 and N9 alkyl derivs. of purine, and to novel compds., namely N7 alkyl derivs. of purine endowed with a potential antiviral or antitumor activity, is described. This new process enables the regioselective coupling of a specific alkyl group in 7 or 9 position of purine. Thus, 4-acetoxy-3-acetoxymethylbutyl tosylate was added to N2-acetyl-7-benzylguanine (preparation given), then reacted with Pd/C to give 9-(4-hydroxy-3-(hydroxymethyl)butyl)guanine in 47% yield.

IT **104227-87-4P, Famciclovir**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); IMF (Industrial manufacture); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**preparation** of alkyl substituted purine derivs. via regioselective coupling)

RN 104227-87-4 CAPLUS

CN 1,3-Propanediol, 2-[2-(2-amino-9H-purin-9-yl)ethyl]-, diacetate (ester) (9CI) (CA INDEX NAME)



REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 31 OF 66 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2000:35368 CAPLUS

DOCUMENT NUMBER: 132:260220

TITLE: Pharmacokinetics and relative bioavailability of famciclovir capsule and famciclovir tablet

AUTHOR(S): Feng, Xia; Wang, Jian-Hua; Zhou, Yan; Tang, Cheng; He, Lei

CORPORATE SOURCE: Department of Clinical Pharmacology, Sun Yet-Sen University of Medical Science, Guang Zhou, 510089, Peop. Rep. China

SOURCE: Zhongguo Linchuang Yaolixue Zazhi (1999), 15(5), 346-351
CODEN: ZLYZE9; ISSN: 1001-6821

PUBLISHER: Beijing Yike Daxue, Linchuang Yaoli Yanjiuso

DOCUMENT TYPE: Journal

LANGUAGE: Chinese

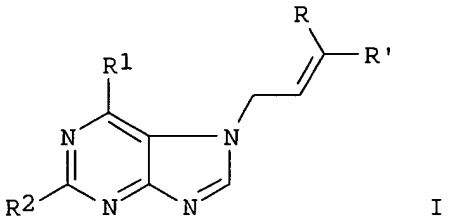
AB A single oral dose [250 mg] of domestic **famciclovir** capsules, domestic **famciclovir** tablets or imported **famciclovir** tablets was given to 9 healthy male volunteers at 1 wk intervals in a three-way randomized cross-over design and blood and urine samples were withdrawn up to 12 h and 24 h, resp. **Famciclovir** was deacetylated and oxidized rapidly to form penciclovir after oral administration. Plasma and urine concns. of penciclovir were determined with HPLC. Two-compartment model with first order absorption was fitted to the concentration-time profiles of these three **prepns.** The results showed that the mean Tmax of these three **prepns.** were 0.47 ± 0.13 h, 0.93 ± 0.40 h and 0.84 ± 0.34 h; Cmax were 2.34 ± 0.47 mg·L-1, 2.20 ± 0.39 mg·L-1 and 2.22 ± 0.66

mg·L-1; the plasma half-lives (T1/2β) were about 3 h; and AUC0-12h were 5.88 ± 0.71 mg·h·L-1, 6.24 ± 1.28 mg·h·L-1 and 6.25 ± 1.24 mg·h·L-1, AUC0-ω were 6.98 ± 0.96 mg·h·L-1, 6.82 ± 1.10 mg·h·L-1 and 7.08 ± 1.08 mg·h·L-1, resp. The accumulating excretion rate of penciclovir in urine in 24 h were 67.1 ± 14.6%, 64.6 ± 11.5% and 64.3 ± 10.1% resp. There was no statistically difference (P>0.05) among these three **prepns.** in the above parameters except Tmax. The relative bioavailability of domestic capsule and domestic tablet was 95.7 + 11.7% and 100.8 ± 15.2% resp., the result of two one-sided test suggest that these two domestic **prepns.** are bioequivalence with the imported tablet.

L5 ANSWER 32 OF 66 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:659387 CAPLUS
DOCUMENT NUMBER: 131:286768
TITLE: Preparation of N-9-alkylated purine derivatives
INVENTOR(S): Geen, Graham Richard; Share, Andrew Colin
PATENT ASSIGNEE(S): Smithkline Beecham Plc, UK
SOURCE: PCT Int. Appl., 19 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 9951604	A2	19991014	WO 1999-EP2309		19990330
WO 9951604	A3	20000217			
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
CA 2323965	AA	19991014	CA 1999-2323965		19990330
AU 9936051	A1	19991025	AU 1999-36051		19990330
BR 9908959	A	20001205	BR 1999-8959		19990330
EP 1068210	A2	20010117	EP 1999-917959		19990330
EP 1068210	B1	20040602			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
JP 2002510692	T2	20020409	JP 2000-542325		19990330
CN 1125068	B	20031022	CN 1999-804402		19990330
AT 268332	E	20040615	AT 1999-917959		19990330
ES 2222702	T3	20050201	ES 1999-917959		19990330
US 6437125	B1	20020820	US 2000-623700		20001101
HK 1035896	A1	20050415	HK 2001-105016		20010717
PRIORITY APPLN. INFO.:			GB 1998-7116	A	19980402
			WO 1999-EP2309	W	19990330

OTHER SOURCE(S): CASREACT 131:286768; MARPAT 131:286768
GI



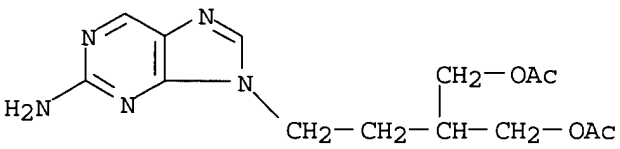
I

AB A method of rearranging N-7-alkylated purines [I; R, R' = H, C1-12 alkyl; R1, R2 = H, OH, halo, C1-12 alkyl, C2-12 alkenyl, (hetero)aryl, C1-12 alkyl- or aryl carbonate, amino, etc.] to form virucidal N-9-alkylated analogs by use of a Pd(0) catalyst in combination with a (diphenylphosphino)nC1-6 alkane (n = 1-6) is claimed. The invention also provides methods of making penciclovir and **famciclovir** using this rearrangement reaction. For example, stirring 2-amino-6-chloropurine and Me 2,2-dimethyl-5-ethenyl-1,3-dioxane-5-carbonate (**preparation** from 2,2-dimethyl-1,3-dioxan-5-one, CH2:CHMgBr and ClCO2Me in 73% yield given) at 60° in DMF in the presence of 1,2-bis(diphenylphosphino)ethane and tris(dibenzylidene) dipalladium(0)·CHCl3 compound gave 61% 5-[2-(2-amino-6-chloropurin-9-yl)]ethylidene-2,2-dimethyl-1,3-dioxane which was hydrogenated for 18 h at 50° in EtOAc in the presence of Pd/C and Et3N to give 74% 5-[2-(2-aminopurin-9-yl)ethyl]-2,2-dimethyl-1,3-dioxane. Acid hydrolysis of the latter with HCl in MeOH/THF gave 81% 2-amino-9-(4-hydroxy-3-hydroxymethylbut-1-yl)purine-HCl which was acetylated with Ac2O in CH2Cl2 the presence of 4-dimethylaminopyridine and Et3N to give 70% **famciclovir.**

IT **104227-87-4P, Famciclovir**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**preparation** of N-9-alkylated purine derivs. as virucides)

RN 104227-87-4 CAPLUS

CN 1,3-Propanediol, 2-[2-(2-amino-9H-purin-9-yl)ethyl]-, diacetate (ester) (9CI) (CA INDEX NAME)



L5 ANSWER 33 OF 66 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1999:659386 CAPLUS

DOCUMENT NUMBER: 131:286640

TITLE: Process for the production of purine derivatives and intermediates

INVENTOR(S): Freer, Richard; Geen, Graham Richard; Ramsay, Thomas Weir; Share, Andrew Colin; Smith, Neil Michael

PATENT ASSIGNEE(S): Smithkline Beecham Plc, UK

SOURCE: PCT Int. Appl., 21 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

Prepared by: Mary Hale @2-2507 Rem Bldg 1D86

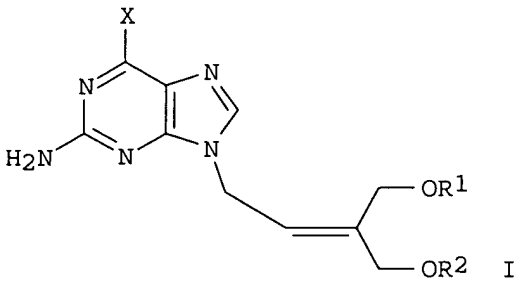
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9951603	A1	19991014	WO 1999-EP2308	19990330
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2322583	AA	19991014	CA 1999-2322583	19990330
AU 9934200	A1	19991025	AU 1999-34200	19990330
BR 9908964	A	20001205	BR 1999-8964	19990330
EP 1068209	A1	20010117	EP 1999-915738	19990330
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002510691	T2	20020409	JP 2000-542324	19990330
US 6555685	B1	20030429	US 2000-623662	20001101
US 2003130512	A1	20030710	US 2003-369841	20030219
US 6806375	B2	20041019		

PRIORITY APPLN. INFO.:

GB 1998-7114	A	19980402
WO 1999-EP2308	W	19990330
US 2000-623662	A3	20001101

OTHER SOURCE(S): CASREACT 131:286640; MARPAT 131:286640
GI



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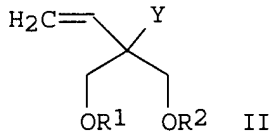


II

AB A process for the production of a compound of formula (I) (X = H, OH or halo; R1, R2 independently = alkyl, aryl, alkylaryl, alkylsilyl, arylsilyl, alkylarylsilyl, or R1, R2 are joined together to form a cyclic acetal or ketal) is presented. The method comprises reacting a 2-amino-6-hydroxy or halopurine with a compound of formula (II) (Y = a leaving group) in the presence of a palladium(0) catalyst and a ligand. The process provides a novel method for the production of famciclovir and penciclovir.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 34 OF 66 CAPLUS COPYRIGHT 2005 ACS on STN

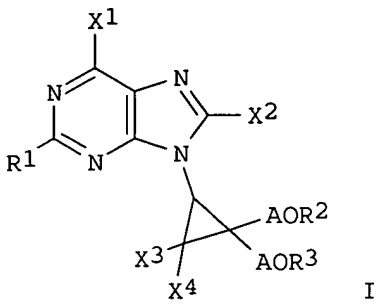
ACCESSION NUMBER: 1999:448609 CAPLUS
DOCUMENT NUMBER: 131:130201
TITLE: An economical synthesis of famciclovir
AUTHOR(S): Hijiya, Toyoto; Yamashita, Keizo; Kojima, Mitsuhiko; Uchida, Yumiko; Katayama, Satoshi; Torii, Takayoshi; Shiragami, Hiroshi; Izawa, Kunisuke
CORPORATE SOURCE: AminoScience Laboratories, Ajinomoto Co. Inc., Kawasaki, 210-8681, Japan
SOURCE: Nucleosides & Nucleotides (1999), 18(4 & 5), 653-654
CODEN: NUNUD5; ISSN: 0732-8311
PUBLISHER: Marcel Dekker, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 131:130201
AB An economical synthesis of famciclovir from N-2-acetyl-7-benzylguanine by a novel regioselective alkylation with the diester cyclopropane compound was developed.
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 35 OF 66 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:380903 CAPLUS
DOCUMENT NUMBER: 131:5268
TITLE: Preparation of purine derivatives having cyclopropane ring
INVENTOR(S): Hayashi, Taketo; Yasuoka, Junichi; Nishiura, Akito
PATENT ASSIGNEE(S): Sumika Fine Chemicals Co., Ltd., Japan
SOURCE: Eur. Pat. Appl., 34 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
EP 916674	A1	19990519	EP 1998-309170		19981110
EP 916674	B1	20020508			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO					
JP 11322749	A2	19991124	JP 1998-133349		19980515
JP 2000016993	A2	20000118	JP 1998-182765		19980629
CA 2251481	AA	19990512	CA 1998-2251481		19981026
AU 9889553	A1	19990603	AU 1998-89553		19981028
AU 737518	B2	20010823			
JP 11199584	A2	19990727	JP 1998-307032		19981028
US 6156892	A	20001205	US 1998-184747		19981103
IN 187819	A	20020629	IN 1998-MA2511		19981106
AT 217311	E	20020515	AT 1998-309170		19981110
PT 916674	T	20020930	PT 1998-309170		19981110
ES 2176914	T3	20021201	ES 1998-309170		19981110
BR 9901429	A	20010320	BR 1999-1429		19990511
US 6342603	B1	20020129	US 2000-541724		20000403
IN 189336	A	20030215	IN 2000-MA633		20000807
PRIORITY APPLN. INFO.:			JP 1997-310839	A	19971112
			JP 1998-133349	A	19980515
			JP 1998-182765	A	19980629
			US 1998-184747	A3	19981103

OTHER SOURCE(S): MARPAT 131:5268

GI



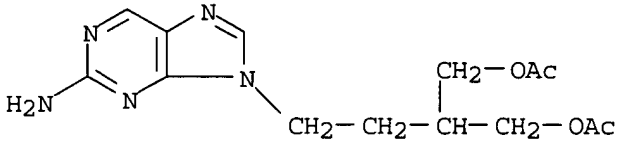
I

AB Cyclopropyl-substituted purine derivs. I (A = CH2, CO; X1 = H, halo, alkoxy, OH; each of X2, X3, and X4 is independently H or halo; R1 = H, halo, protected or unprotected amino group; each of R2 and R3 is independently H or a substituted or unsubstituted alkyl group, a substituted or unsubstituted aralkyl group, or a substituted or unsubstituted acyl group; in a case where A is CO, neither R2 nor R3 is a substituted or unsubstituted acyl group, and each of X3 and X4 is independently halo) were prepared E.g., reaction of 2-amino-6-chloropurine with di-Me 2,2,2-trichloroethylidenemalonate gave 83.4% 2-amino-6-chloro-9-(3,3-dicarbomethoxy-2,2-dichlorocyclopropyl)purine. Treating the latter with H2/Pd under pressure gave 60.0% di-Me 2-(2-(2-aminopurin-9-yl)ethyl)malonate.

IT **104227-87-4P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(**preparation** and reactions of cyclopropyl-substituted purines)

RN 104227-87-4 CAPLUS

CN 1,3-Propanediol, 2-[2-(2-amino-9H-purin-9-yl)ethyl]-, diacetate (ester) (9CI) (CA INDEX NAME)

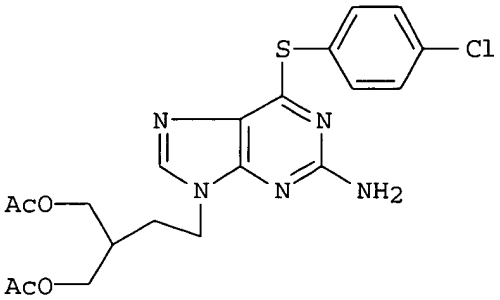


REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 36 OF 66 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:270561 CAPLUS
DOCUMENT NUMBER: 131:5235
TITLE: Convenient syntheses of 9-[4-hydroxy-3-(hydroxymethyl)butyl]guanine (penciclovir) and 9-[4-acetoxy-3-(acetoxymethyl)butyl]-2-amino-9H-purine (famciclovir)
AUTHOR(S): Brand, Briony; Reese, Colin B.; Song, Quanlai; Visintin, Cristina
CORPORATE SOURCE: Department of Chemistry, King's College London,

Prepared by: Mary Hale @2-2507 Rem Bldg 1D86

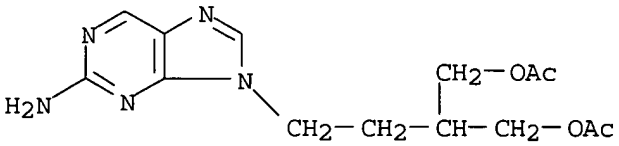
London, WC2R 2LS, UK
SOURCE: Tetrahedron (1999), 55(16), 5239-5252
CODEN: TETRAB; ISSN: 0040-4020
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



III

AB Guanine was converted, in a one pot reaction, to 2-amino-6-[(4-chlorophenyl)thio]purine (I) in 88% isolated yield. 4-Acetoxy-3-(acetoxymethyl)butanol (II) was **prepared** from 2-chloroethanol in five steps and in 46% overall yield. The mesylate ester of II reacted with I in the presence of potassium carbonate with a high degree of regioselectivity (89%) to give the N-9 alkylated product (III), which was isolated in 80% yield. Acidic hydrolysis of III gave penciclovir in virtually quant. yield. Penciclovir and **famciclovir** were **prepared** from I in four and five steps, resp., by procedures involving initial alkylation with 1,2-dibromoethane. The overall yields were 65 and ca. 60%, resp.

IT **104227-87-4P, Famciclovir**
RL: SPN (Synthetic preparation); PREP (Preparation)
(convenient **preparation** of)
RN 104227-87-4 CAPLUS
CN 1,3-Propanediol, 2-[2-(2-amino-9H-purin-9-yl)ethyl]-, diacetate (ester) (9CI) (CA INDEX NAME)



REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 37 OF 66 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:235777 CAPLUS
DOCUMENT NUMBER: 130:282302
TITLE: Synthesis and Evaluation of 2-amino-6-fluoro-9-(4-hydroxy-3-hydroxymethylbut-1-yl)purine mono- and diesters as potential prodrugs of penciclovir
AUTHOR(S): Kim, Dae-Kee; Lee, Namkyu; Kim, Hun-Taek; Im, Guang-Jin; Kim, Key H.

CORPORATE SOURCE: Life Science Research Center, SK Chemicals, Suwon-Si, 440-745, S. Korea
SOURCE: Bioorganic & Medicinal Chemistry (1999), 7(3), 565-570
CODEN: BMECEP; ISSN: 0968-0896
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB 2-Amino-6-fluoro-9-(4-hydroxy-3-hydroxymethylbut-1-yl)purine, and its mono- and diesters were **prepared** and evaluated for their potential as prodrugs of penciclovir. Treatment of 2-amino-6-chloro-9-(4-hydroxy-3-hydroxymethylbut-1-yl)purine with trimethylamine in THF followed by a reaction of the resulting trimethylammonium chloride salt with KF in DMF afforded 2-amino-6-fluoro-9-(4-hydroxy-3-hydroxymethylbut-1-yl)purine in 80% yield. Esterification with an appropriate acid anhydride [Ac2O, (EtCO)2O, (n-PrCO)2O, or (i-PrCO)2O] in DMF in the presence of a catalytic amount of DMAP produced the mono-esters in 42-45% yields and diesters in 87-99% yields. Of the prodrugs tested in rats, the mono-isobutyrate was the most efficiently absorbed and metabolized, showing the mean maximum total concentration of penciclovir (5.5 μg/mL) and 2-Amino-6-fluoro-9-(4-hydroxy-3-hydroxymethylbut-1-yl)purine (10.8 μg/mL) in the blood was much higher than the mean maximum concentration of penciclovir (11.5 μg/mL) from **famciclovir.** However, the mean concns. of penciclovir from the mono-isobutyrate were lower than those from **famciclovir** because of the limited conversion of a major metabolite to penciclovir by adenosine deaminase.

REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 38 OF 66 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:200220 CAPLUS
DOCUMENT NUMBER: 130:237741
TITLE: Graphical synthetic routes of famciclovir
AUTHOR(S): Zhang, Lei; Chen, Ying-Qi; Qian, Guo-Qing; Wu, Hai-Hong; Dai, Li-Yan; Yang, Li-Ping
CORPORATE SOURCE: Dept. of Chemistry, East China Normal University, Shanghai, 200062, Peop. Rep. China
SOURCE: Zhongguo Yiyao Gongye Zazhi (1999), 30(2), 93-96
CODEN: ZYGZEA; ISSN: 1001-8255
PUBLISHER: Zhongguo Yiyao Gongye Zazhi Bianjibu
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Chinese

AB A review with 25 refs. on the synthesis of famciclovir.

L5 ANSWER 39 OF 66 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:803933 CAPLUS
DOCUMENT NUMBER: 130:52738
TITLE: Preparation of modified peptides as isosteric antiherpes agents
INVENTOR(S): Beaulieu, Pierre Louis; Deziel, Robert; Brunet, Montse Llinas; Moss, Neil; Plante, Raymond
PATENT ASSIGNEE(S): Boehringer Ingelheim (Canada) Ltd., Can.
SOURCE: U.S., 24 pp., Cont.-in-part of U.S. 5,574,015.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

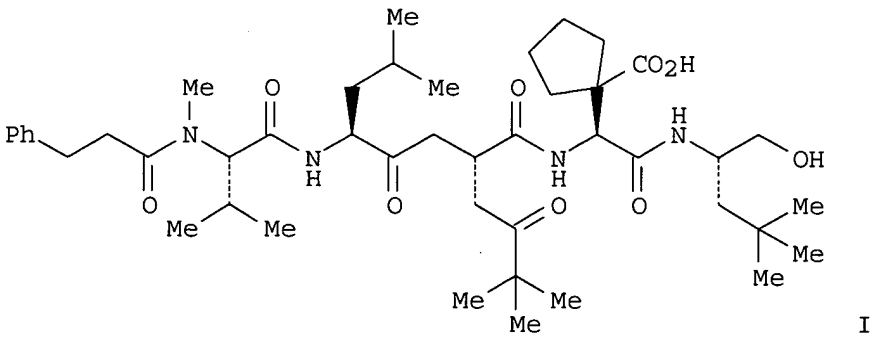
US 5846941	A	19981208	US 1995-460957	19950605
AU 9338807	A1	19931005	AU 1993-38807	19930312
AU 671825	B2	19960912		
BR 9306074	A	19971118	BR 1993-6074	19930312
CA 2131186	C	20001212	CA 1993-2131186	19930312
NO 9403345	A	19940909	NO 1994-3345	19940909
FI 9404187	A	19940912	FI 1994-4187	19940912
US 5574015	A	19961112	US 1994-324434	19941017
CA 2139169	AA	19960629	CA 1994-2139169	19941228
CA 2139169	C	20010501		

PRIORITY APPLN. INFO.:

US 1992-849918	B2	19920312
US 1993-25507	B1	19930303
US 1994-324434	A2	19941017
CA 1994-2139169	A	19941228
WO 1993-CA95	A	19930312

OTHER SOURCE(S): MARPAT 130:52738

GI



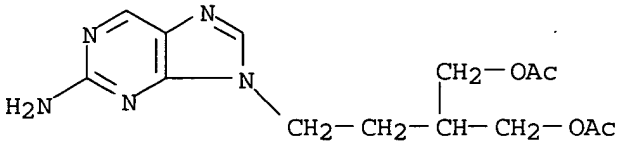
I

AB Disclosed herein are peptidomimetic compds. of the formula A-B-D-CH2CH(CH2COR1)CONHCH(CR2R3CO2H)CO-E [I; A = (substituted) phenylalkyl, phenylalkylaminocarbonyl; B = NMeCHR4CO; R4 = alkyl; A-B = R5NHCO; R55 = alkyl, cycloalkyl, alkylcycloalkyl, 1-(2-propenyl)-3-butenyl, etc.; D = NHCHR6CO; R6 = (substituted) alkyl; R1 = alkyl, cycloalkyl, alkylcycloalkyl, amino; R2 = H, alkyl, R3 = alkyl; or R2 = H, R3 = alkenyl, phenylalkyl; or CR2R3 = cycloalkyl; E = NHR9, NHNR10R11, etc.; R9, R11 = alkyl; R10 = H, alkyl]. The derivs. are useful for treating herpes infections. Thus, modified peptide derivative II, prepared by solution phase methods, inhibited herpes simplex virus (HSV) ribonucleotide reductase with IC50 = 0.27 mM, and inhibited HSV replication in cell culture with EC50 = 15-19 mM. II showed synergistic activity with acyclovir against HSV.

IT **104227-87-4, Famciclovir**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**preparation** of modified peptides as isosteric antiherpes agents)

RN 104227-87-4 CAPLUS

CN 1,3-Propanediol, 2-[2-(2-amino-9H-purin-9-yl)ethyl]-, diacetate (ester) (9CI) (CA INDEX NAME)



REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 40 OF 66 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:708921 CAPLUS
DOCUMENT NUMBER: 129:347286
TITLE: A bioadhesive drug delivery system based on liquid crystals
INVENTOR(S): Nielsen, Lise Sylvest
PATENT ASSIGNEE(S): Dumex-Alpharma A/S, Den.
SOURCE: PCT Int. Appl., 176 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9847487	A1	19981029	WO 1998-DK159	19980417
W: AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, CZ, DE, DE, DK, DK, EE, EE, ES, FI, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2286052	AA	19981029	CA 1998-2286052	19980417
AU 9869195	A1	19981113	AU 1998-69195	19980417
EP 975331	A1	20000202	EP 1998-914850	19980417
R: CH, DE, DK, ES, FR, GB, IT, LI, NL				
JP 2001524958	T2	20011204	JP 1998-544757	19980417
PRIORITY APPLN. INFO.:			DK 1997-435 A	19970417
			WO 1998-DK159 W	19980417

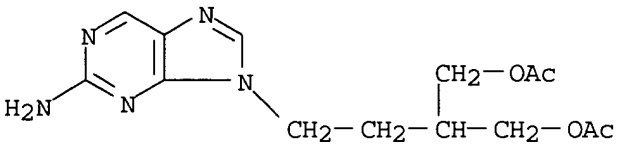
AB A drug delivery system containing a liquid crystalline phase such as a cubic, a hexagonal, a reverse hexagonal, a lamellar, a micellar and a reverse micellar liquid crystalline phase is disclosed. The compns. are unique in that they, as delivery systems, contain (A) a substance which is capable of generating a liquid crystalline phase and providing suitable biopharmaceutical properties, e.g. suitable release of the active substance and bioadhesive properties, and (B) at least another substance which, without having any substantially neg. effect on the biopharmaceutical properties provided by the substance mentioned above under (A), either takes part in the formation of a liquid crystalline phase or dils. the proportion of liquid crystalline phase in the composition while still maintaining suitable biopharmaceutical properties and a suitable storage stability. Examples of substances A are fatty acid esters, e.g. glycerylmonooleate and glycerylmonolinoleate, and examples of substances B are structurants, e.g. phospholipids and

tocopherols and/or pharmaceutically acceptable excipients.

IT **104227-87-4, Famciclovir**
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(bioadhesive drug delivery system based on liquid **crystals**)

RN 104227-87-4 CAPLUS

CN 1,3-Propanediol, 2-[2-(2-amino-9H-purin-9-yl)ethyl]-, diacetate (ester) (9CI) (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 41 OF 66 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:361446 CAPLUS
DOCUMENT NUMBER: 129:136409
TITLE: Practical synthesis of antiviral nucleosides
AUTHOR(S): Izawa, Kunisuke; Shiragami, Hiroshi
CORPORATE SOURCE: Central Res. Lab., Alinomoto Co. Inc., Kawasaki, 210, Japan
SOURCE: Pure and Applied Chemistry (1998), 70(2), 313-318
CODEN: PACHAS; ISSN: 0033-4545
PUBLISHER: Blackwell Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Guanosine produced by fermentation is one of the nucleosides most readily available on an industrial scale. We have recently developed several processes leading to known antiviral agents starting with guanosine. The processes involve enzymic transglycosylation for stavudine (d4T), chemical transpurination for acyclovir and ganciclovir, and novel alkylation for penciclovir and famciclovir.

REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 42 OF 66 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:233225 CAPLUS
DOCUMENT NUMBER: 128:316788
TITLE: Hepatitis B and C viruses: molecular identification and targeted antiviral therapies
AUTHOR(S): Berenguer, Marina; Wright, Teresa L.
CORPORATE SOURCE: Department of Veterans Affairs Medical Center, University of California, San Francisco, CA, 94121, USA
SOURCE: Proceedings of the Association of American Physicians (1998), 110(2), 98-112
CODEN: PAAPFD; ISSN: 1081-650X
PUBLISHER: Blackwell Science, Inc.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 77 refs. Four agents are in clin. development for the treatment of chronic hepatitis B (HBV) infection. These nucleoside analogs are incorporated into the growing DNA chain and terminate

replication. Lamivudine, a cytidine analog that inhibits the synthesis of neg. strand DNA from pre-genomic RNA, predictably inhibits replication and improves liver enzymes and histol. in infected individuals. Following cessation of treatment, relapse is common, and genetic causes of viral resistance have been described. Other drugs for HBV infection include **famciclovir**, a guanosine analog that has also shown to suppress replication in immunocompetent as well as in immunocompromised patients; lobucavir, a guanosine analog; and adefovir, an adenine nucleotide analog. The future of drug therapy against HBV likely includes combination agents with one or more nucleoside/nucleotide analogs and immune stimulants, such as interferon, or therapeutic vaccines. Recent advances in the treatment of hepatitis C (HCV) have been less impressive. An effective vaccine is greatly needed yet development in the near future is unlikely. Recommendations for therapy of chronic HCV have been proposed following the National Institutes of Health Consensus Conference. Interferon alpha is advised in patients with elevated serum alanine aminotransferases and liver histol. demonstrating active hepatitis, regardless of level of pretreatment viremia or infecting genotype. Therapy should be continued for three months, at which time response should be assessed. If a biochem. and/or virol. response has been achieved, treatment should be continued for a year. Trials are underway to evaluate interferon in combination with ribavirin. Recent identification of the **crystalline** structure of the HCV NS3 protease promises development of effective inhibitors of this critical viral enzyme.

REFERENCE COUNT: 77 THERE ARE 77 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 43 OF 66 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1997:719675 CAPLUS
DOCUMENT NUMBER: 127:346611
TITLE: Process for the preparation of purine derivatives as antiviral agents
INVENTOR(S): Geen, Graham Richard; Jarvest, Richard Lewis
PATENT ASSIGNEE(S): Beecham Group PLC, UK
SOURCE: U.S., 3 pp., Cont.-in-part of U.S. Ser. No. 132,082, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

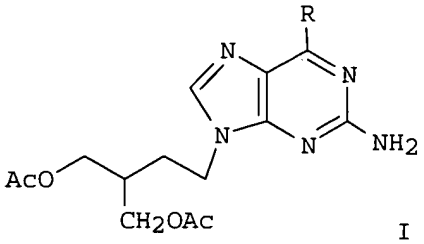
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5684153	A	19971104	US 1994-258167	19940610
US 5075445	A	19911224	US 1987-85216	19870812
US 5246937	A	19930921	US 1992-824131	19920122
US 5250688	A	19931005	US 1992-825440	19920122
US 6579981	B1	20030617	US 1994-311291	19940923
US 6573378	B1	20030603	US 1994-357363	19941215
US 5886215	A	19990323	US 1997-884731	19970630
US 6187922	B1	20010213	US 1999-238777	19990127
US 2001004668	A1	20010621	US 2000-734051	20001211
US 6388074	B2	20020514		

PRIORITY APPLN. INFO.:

US 1984-641300	B1 19840816
US 1985-777188	B1 19850918
US 1987-85216	A3 19870812
US 1988-285399	B1 19881215
US 1990-607403	B1 19901031

US 1992-825440	A1	19920122
US 1992-918111	B2	19920720
US 1993-132082	B2	19931005
GB 1983-22199	A	19830818
GB 1983-25271	A	19830921
GB 1984-8322	A	19840330
GB 1984-23833	A	19840920
GB 1985-10331	A	19850423
GB 1985-20618	A	19850816
US 1991-697853	B1	19910509
US 1991-285399	B3	19911206
US 1992-847833	B1	19920309
US 1994-258167	A3	19940610
US 1997-884731	A3	19970630
US 1999-238777	A3	19990127

OTHER SOURCE(S): CASREACT 127:346611
GI



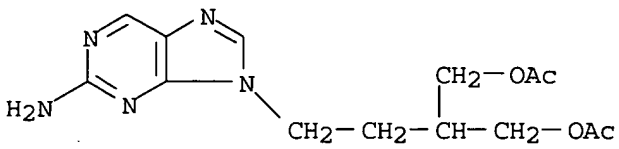
I

AB The present invention provides a process for the synthesis of penciclovir (I; R = OH) and famciclovir (I; R = H) by N9-alkylating 2-amino-6-chloropurine with 2-(acetoxymethyl)-4-(leaving group)-but-1-yl acetate (leaving group = Cl, Br, I) to give purine I (R = Cl), followed by hydrolysis or reduction, resp. Thus, 2-amino-6-chloropurine is reacted with (acetoxymethyl)iodobut-1-yl acetate in DMF containing K2CO3 to give 75% I (R = Cl) and 15% of N7-isomer. I (R = OH, H) are antiviral agents.

IT **104227-87-4P, Famciclovir**
RL: PNU (Preparation, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**preparation** of purine derivs. as antiviral agents)

RN 104227-87-4 CAPLUS

CN 1,3-Propanediol, 2-[2-(2-amino-9H-purin-9-yl)ethyl]-, diacetate (ester) (9CI) (CA INDEX NAME)



L5 ANSWER 44 OF 66 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:513561 CAPLUS
DOCUMENT NUMBER: 127:171594
TITLE: Nucleoside analogs in combination therapy of herpes

simplex infections
INVENTOR(S): Boyd, Malcolm Richard
PATENT ASSIGNEE(S): Smithkline Beecham Plc, UK; Boyd, Malcolm Richard
SOURCE: PCT Int. Appl., 12 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 9726882	A1	19970731	WO 1997-GB226		19970124
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG					
CA 2244268	AA	19970731	CA 1997-2244268		19970124
AU 9715506	A1	19970820	AU 1997-15506		19970124
AU 713202	B2	19991125			
ZA 9700608	A	19980724	ZA 1997-608		19970124
EP 876146	A1	19981111	EP 1997-901694		19970124
EP 876146	B1	20030502			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
CN 1209748	A	19990303	CN 1997-191869		19970124
CN 1133433	B	20040107			
BR 9707304	A	19990720	BR 1997-7304		19970124
JP 2000507211	T2	20000613	JP 1997-526681		19970124
NZ 326839	A	20010223	NZ 1997-326839		19970124
IL 125075	A1	20030212	IL 1997-125075		19970124
AT 238796	E	20030515	AT 1997-901694		19970124
PT 876146	T	20030930	PT 1997-901694		19970124
ES 2199339	T3	20040216	ES 1997-901694		19970124
PL 187076	B1	20040531	PL 1997-327917		19970124
TW 493985	B	20020711	TW 1997-86102357		19970226
NO 9803402	A	19980723	NO 1998-3402		19980723
NO 316355	B1	20040119			
HK 1016475	A1	20031205	HK 1999-101446		19990409
US 6514980	B1	20030204	US 2000-626015		20000726
US 2004185433	A1	20040923	US 2001-884715		20010619
PRIORITY APPLN. INFO.:			GB 1996-1544	A	19960126
			WO 1997-GB226	W	19970124
			US 1998-117154	B3	19980724

AB A pharmaceutical product comprising a nucleoside analog active against herpes simplex virus, such as acyclovir/valaciclovir or penciclovir/ **famciclovir**, and an immunosuppressant, as a combined **prepn** . for simultaneous, sep. or sequential use in the treatment and/or prevention of herpes simplex virus infections. Cyclosporin A in combination with **famciclovir** or valaciclovir had greater effects in mice than the nucleosides alone.

L5 ANSWER 45 OF 66 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:499104 CAPLUS
DOCUMENT NUMBER: 127:166845

TITLE: High-content famciclovir tablets
INVENTOR(S): Greenway, Michael John; Slater, Jennifer Mary
PATENT ASSIGNEE(S): Smithkline Beecham Plc, UK; Greenway, Michael John; Slater, Jennifer Mary
SOURCE: PCT Int. Appl., 8 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9725990	A1	19970724	WO 1997-EP195	19970113
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2240462	AA	19970724	CA 1997-2240462	19970113
AU 9715418	A1	19970811	AU 1997-15418	19970113
AU 713090	B2	19991125		
EP 874632	A1	19981104	EP 1997-901539	19970113
EP 874632	B1	20020724		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO				
CN 1208350	A	19990217	CN 1997-191703	19970113
CN 1132582	B	20031231		
BR 9706982	A	19990720	BR 1997-6982	19970113
JP 2000503311	T2	20000321	JP 1997-525692	19970113
NZ 326769	A	20000526	NZ 1997-326769	19970113
CZ 287205	B6	20001011	CZ 1998-2254	19970113
SK 282132	B6	20011106	SK 1998-956	19970113
AT 220910	E	20020815	AT 1997-901539	19970113
AP 1114	A	20021018	AP 1998-1298	19970113
W: KE, LS, MW, SD, SZ, UG, GH, GM, ZW				
PT 874632	T	20021031	PT 1997-901539	19970113
ES 2180922	T3	20030216	ES 1997-901539	19970113
PL 187291	B1	20040630	PL 1997-327922	19970113
TW 434016	B	20010516	TW 1997-86100335	19970114
ZA 9700310	A	19971023	ZA 1997-310	19970115
NO 9803259	A	19980715	NO 1998-3259	19980715
NO 315689	B1	20031013		
BG 63488	B1	20020329	BG 1998-102638	19980715
US 6765007	B1	20040720	US 1998-101926	19980924
HK 1016473	A1	20030509	HK 1999-101423	19990408
PRIORITY APPLN. INFO.:			GB 1996-847 A	19960116
			WO 1997-EP195 W	19970113

AB A **famciclovir** tablet in which the percentage of the drug by in the tablet is ≥85% by et. is described. Thus, tablets were **prepared** from famicyclovir 91.42, hydroxypropyl cellulose 2.83, sodium starch glycolate 5.00, Mg stearate 0.75, and anhydrous lactose 0%.

L5 ANSWER 46 OF 66 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:356544 CAPLUS
DOCUMENT NUMBER: 126:334374

Prepared by: Mary Hale @2-2507 Rem Bldg 1D86

TITLE: A pharmaceutical composition for administration of an active substance to or through skin or mucosal surface
INVENTOR(S): Nielsen, Lise Sylvest; Hansen, Jens
PATENT ASSIGNEE(S): Dumex-Alpharma A/s, Den.; Nielsen, Lise Sylvest; Hansen, Jens
SOURCE: PCT Int. Appl., 103 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9713528	A1	19970417	WO 1996-DK437	19961011
W: AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, CZ, DE, DE, DK, DK, EE, EE, ES, FI, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC				
CA 2231273	AA	19970417	CA 1996-2231273	19961011
AU 9672792	A1	19970430	AU 1996-72792	19961011
AU 702030	B2	19990211		
EP 871489	A1	19981021	EP 1996-934441	19961011
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 11513393	T2	19991116	JP 1996-514651	19961011
NO 9801633	A	19980604	NO 1998-1633	19980408
FI 9800822	A	19980409	FI 1998-822	19980409
PRIORITY APPLN. INFO.:			DK 1995-1150 A	19951012
			WO 1996-DK437 W	19961011

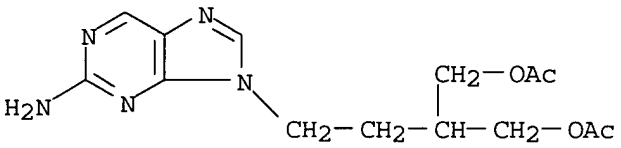
AB Pharmaceutical compns. for administration of an active substance to or through a damaged or undamaged skin or mucosal surface or to the oral cavity including the teeth of an animal such as a human. The composition has advantageous properties with respect to release of the active substance form the composition and, furthermore, the composition is bioadhesive. The composition comprises the active substance and an effective amount of a fatty acid ester which, together with a liquid phase, is capable of generating a liquid **crystalline** phase in which the constituents of the composition are enclosed, the active substance having a solubility in the liquid **crystalline** phase of at most 20 mg/g at 20°C, and a solubility in water of at most 10 mg/mL at 20°C, the water, where applicable, being buffered to a pH substantially identical to the pH prevailing in the liquid **crystalline** phase (pH about 3.6-9). The composition is particularly suited for administration of substances which have a very low water solubility and which are to be supplied in an effective amount in a localized region over a period of time. Active substances of particular importance are antiherpes virus agents including antiviral drugs and prodrugs thereof, such as nucleosides, nucleoside analogs, phosphorylated nucleosides (nucleotides), nucleotide analogs and salts, complexes and prodrugs thereof; e.g. guanosine analogs, deoxyguanosine analogs, guanine, guanine analogs, thymidine analogs, uracil analogs and adenine analogs. Especially interesting antiherpes virus agents for use either alone or in combination in a composition according to the present invention are selected from acyclovir, **famciclovir**, desciclovir, penciclovir, zidovudine, ganciclovir, didanosine, zalcitabine, valaciclovir, sorivudine, lobucavir, brivudine,

cidofovir, n-docosanol, ISIS-2922, and prodrugs and analogs thereof.

IT **104227-87-4, Famciclovir**
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(liquid **crystal** pharmaceutical composition for administration of an active substance to or through skin or mucosal surface)

RN 104227-87-4 CAPLUS

CN 1,3-Propanediol, 2-[2-(2-amino-9H-purin-9-yl)ethyl]-, diacetate (ester) (9CI) (CA INDEX NAME)

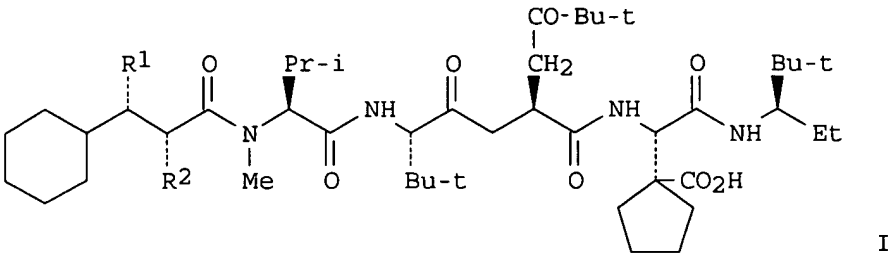


L5 ANSWER 47 OF 66 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1997:155109 CAPLUS
DOCUMENT NUMBER: 126:157826
TITLE: Preparation of peptides as herpes ribonucleotide reductase inhibitors
INVENTOR(S): Gauthier, Jean-Andre; Moss, Neil
PATENT ASSIGNEE(S): Bio-Mega/Boehringer Ingelheim Research Inc., Can.
SOURCE: PCT Int. Appl., 63 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 9700855	A1	19970109	WO 1996-CA180		19960327
W: AU, BR, BY, CN, CZ, EE, HU, JP, KR, LT, LV, MX, NO, NZ, PL, RU, SG, SI, SK, UA					
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
CA 2152541	AA	19961224	CA 1995-2152541		19950623
CA 2152541	C	19981215			
AU 9650977	A1	19970122	AU 1996-50977		19960327
EP 837845	A1	19980429	EP 1996-907230		19960327
EP 837845	B1	20011128			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
JP 11508246	T2	19990721	JP 1996-503484		19960327
AT 209628	E	20011215	AT 1996-907230		19960327
US 5672586	A	19970930	US 1996-666732		19960618
ZA 9605272	A	19961223	ZA 1996-5272		19960621
PRIORITY APPLN. INFO.:			CA 1995-2152541	A	19950623
			WO 1996-CA180	W	19960327

OTHER SOURCE(S): MARPAT 126:157826
GI



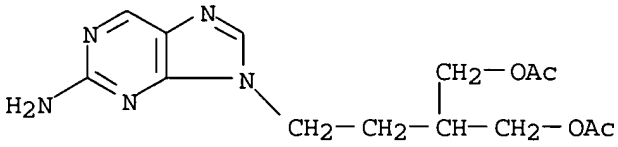
I

AB Peptides I (R1 = H, alkyl; R2 = alkyl) or their therapeutically acceptable salts were prepared for use in the treatment of herpes infections. Thus, treatment of H-(N-Me)Val-Tbg-CH2-(R)-CH(CH2COCMe3)CO-Asp(cyPn)(CH2Ph)-NH-(R)-CHEtCMe3 [(N-Me)Val represents the residue of (S)-2-(methylamino)-3-methylbutanoic acid, Tbg represents the residue of (S)-2-amino-3,3-dimethylbutanoic acid, and Asp(cyPn) represents the residue of (S)-α-amino-1-carboxycyclopentaneacetic acid] (synthesis described) with α(R)-methylcyclohexanepropionic acid chloride in CH2Cl2 in the presence of N-methylmorpholine, followed by hydrogenolysis to remove to benzyl group, afforded I (R1 = H, R2 = Me). The latter peptide inhibited HSV-1 ribonucleotide reductase (IC50 = 0.147 μM). Synergistic combinations of I and acyclovir against HSV-1 are described.

IT **104227-87-4, Famciclovir**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**preparation** of peptides as herpes ribonucleotide reductase inhibitors)

RN 104227-87-4 CAPLUS

CN 1,3-Propanediol, 2-[2-(2-amino-9H-purin-9-yl)ethyl]-, diacetate (ester) (9CI) (CA INDEX NAME)



L5 ANSWER 48 OF 66 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1996:537627 CAPLUS

DOCUMENT NUMBER: 125:196390

TITLE: Antiherpes peptidomimetic compounds

INVENTOR(S): Deziel, Robert; Brunet, Montse Llinas; Moss, Neil; Plante, Raymond

PATENT ASSIGNEE(S): Bio-Mega/boehringer Ingelheim Research Inc., Can.

SOURCE: PCT Int. Appl., 61 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9620171	A1	19960704	WO 1995-CA626	19951031

Prepared by: Mary Hale @2-2507 Rem Bldg 1D86

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RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

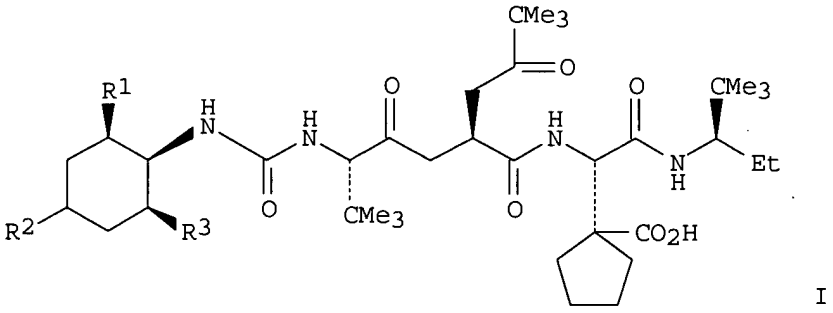
CA 2139169	AA	19960629	CA 1994-2139169		19941228
CA 2139169	C	20010501			
CA 2230750	AA	19960629	CA 1994-2230750		19941228
CA 2230750	C	20020521			
AU 9537395	A1	19960719	AU 1995-37395		19951031
EP 800512	A1	19971015	EP 1995-935318		19951031
EP 800512	B1	20000105			

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE

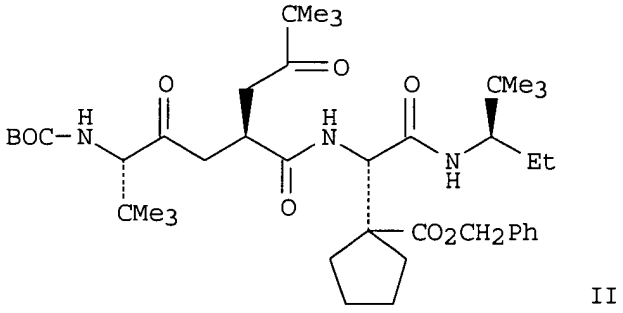
TW 432035	B	20010501	TW 1995-84112900		19951204
ZA 9510964	A	19960608	ZA 1995-10964		19951227
PRIORITY APPLN. INFO.:			CA 1994-2139169	A	19941228
			WO 1995-CA626	W	19951031

OTHER SOURCE(S): MARPAT 125:196390

GI



I

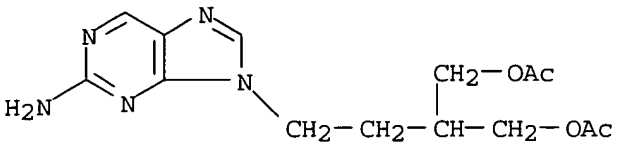


II

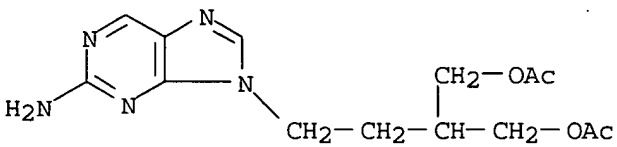
AB Title compds. I [R1 = C1-3 alkyl; R2 = H, C1-2 alkyl; R3 = C1-3 alkyl] and their therapeutically acceptable salts are disclosed. The compds. are useful for treating herpes infections. For example, (R)-1-ethyl-2,2-dimethylpropylamine-HCl and (S)-α-azido-1-[(phenylmethoxy)carbonyl]cyclopentaneacetic acid (prepns. given) were converted in several steps to intermediate II, which was N-deprotected, treated with the corresponding dimethylisocyanatocyclohexane isomer, and fully deprotected by hydrogenolysis to give title compound I [R1 = R3 = Me, R2 = H] (III). In tests against Herpes simplex virus HSV-2 replication in cell culture, III had EC50 of 7 μM. In similar tests against HSV-1, acyclovir and III had EC50 values of 2.2 and 2.3 μM alone, whereas a mixture of acyclovir and 2.0 μM III (the EC30) had an EC50 of 0.12 μM.

Prepared by: Mary Hale @2-2507 Rem Bldg 1D86

IT **104227-87-4D, Famciclovir**, mixts. with peptidomimetics
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(synergistic compns.; **preparation** of peptidomimetics as antivirals for herpes infections)
RN 104227-87-4 CAPLUS
CN 1,3-Propanediol, 2-[2-(2-amino-9H-purin-9-yl)ethyl]-, diacetate (ester) (9CI) (CA INDEX NAME)



L5 ANSWER 49 OF 66 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:278107 CAPLUS
DOCUMENT NUMBER: 125:34011
TITLE: A direct approach to the synthesis of famciclovir and penciclovir
AUTHOR(S): Choudary, Bernadette M.; Geen, Graham R.; Kincey, Peter M.; Parratt, Martin J.; Dales, J. Robert M.; Johnson, Graham P.; O'Donnell, Steven; Tudor, David W.; Woods, Neil
CORPORATE SOURCE: SmithKline Beecham Pharmaceuticals, Harlow, CM19 5AW, UK
SOURCE: Nucleosides & Nucleotides (1996), 15(5), 981-994
CODEN: NUNUD5; ISSN: 0732-8311
PUBLISHER: Dekker
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Reaction of 2-amino-6-chloropurine with tri-Et 3-bromopropane-1,1,1-tricarboxylate followed by decarbethoxylation/transesterification of the unpurified product was the key sequence in synthesizing both the anti-herpesvirus agent penciclovir and its oral form famciclovir in three isolated steps.
IT **104227-87-4P, Famciclovir**
RL: SPN (Synthetic preparation); PREP (Preparation)
(**preparation** of **famciclovir** and penciclovir)
RN 104227-87-4 CAPLUS
CN 1,3-Propanediol, 2-[2-(2-amino-9H-purin-9-yl)ethyl]-, diacetate (ester) (9CI) (CA INDEX NAME)



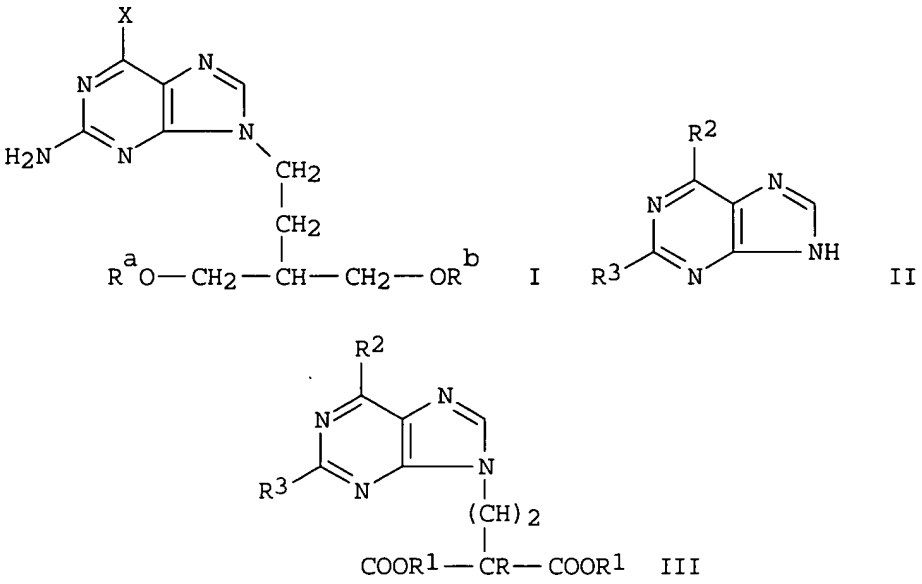
L5 ANSWER 50 OF 66 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:998137 CAPLUS
DOCUMENT NUMBER: 124:86711

TITLE: Preparation of antiviral purine derivatives
INVENTOR(S): Dales, John Robert Mansfield
PATENT ASSIGNEE(S): SmithKline Beecham PLC, UK
SOURCE: PCT Int. Appl., 11 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9528402	A2	19951026	WO 1995-EP1840	19950419
WO 9528402	A3	19960125		
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
ZA 9503110	A	19960520	ZA 1995-3110	19950418
IL 113409	A1	19990817	IL 1995-113409	19950418
IN 183830	A	20000429	IN 1995-DE705	19950418
CA 2188181	AA	19951026	CA 1995-2188181	19950419
AU 9526706	A1	19951110	AU 1995-26706	19950419
AU 691000	B2	19980507		
EP 756597	A1	19970205	EP 1995-921751	19950419
EP 756597	B1	20010516		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
CN 1150427	A	19970521	CN 1995-193489	19950419
CN 1045963	B	19991027		
HU 75339	A2	19970528	HU 1996-2891	19950419
BR 9507494	A	19970812	BR 1995-7494	19950419
JP 09512000	T2	19971202	JP 1995-526738	19950419
EG 20938	A	20000628	EG 1995-326	19950419
RU 2158266	C2	20001027	RU 1996-121936	19950419
CZ 287674	B6	20010117	CZ 1996-3053	19950419
PL 181219	B1	20010629	PL 1995-316943	19950419
ES 2158948	T3	20010916	ES 1995-921751	19950419
PT 756597	T	20011130	PT 1995-921751	19950419
SK 283193	B6	20030304	SK 1996-1332	19950419
RO 118950	B1	20040130	RO 1996-2001	19950419
NO 9604395	A	19961015	NO 1996-4395	19961015
NO 315000	B1	20030623		
FI 9604193	A	19961218	FI 1996-4193	19961018
BG 63464	B1	20020228	BG 1996-100926	19961018
HK 1012348	A1	20020412	HK 1998-113459	19981215
US 6846927	B1	20050125	US 1999-265926	19990311
GR 3036338	T3	20011130	GR 2001-401190	20010807
US 2005101570	A1	20050512	US 2004-11352	20041214

PRIORITY APPLN. INFO.:	GB 1994-7698	A	19940419
	WO 1995-EP1840	W	19950419
	US 1996-732479	B1	19961018
	US 1999-265926	A1	19990311

OTHER SOURCE(S): CASREACT 124:86711; MARPAT 124:86711
GI

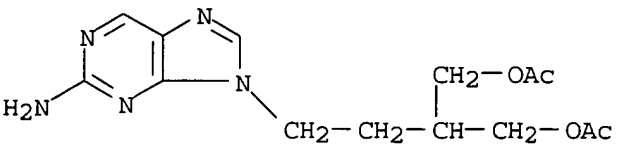


AB The title compds. [I; X is hydrogen, hydroxy, chloro, C1-6 alkoxy or Ph-C1-6 alkoxy; and Ra and Rb are hydrogen, or acyl or phosphate derivs. thereof] are **prepared** via reaction of II [R2 is hydrogen, hydroxy, chlorine, C1-6 alkoxy, Ph C1-6 alkoxy or amino; R3 is halogen, C1-6 alkylthio, C1-6 alkylsulfonyl, azido, an amino group or a protected amino group] with L-(CH2)2-C(COOR1)3 wherein L is a leaving group and R1 is C1-6 alkyl, or Ph-C1-6 alkyl in which the Ph group is optionally substituted to give III [R = COOR1; R1-R3 same as above], decarboxylation of the latter to give III [R = H; R1-R3 same as above], followed by conversion of the latter to I. Thus, coupling of II [R2 = Cl, R3 = NH2] with Br-CH2-CH2-C(CO2Et)3 followed by decarboxylation gave III [R = H, R1 = Et, R2 = Cl, R3 = NH2], which was reduced with NaBH4 and then acetylated to give I [X = Cl, Ra = Rb = Ac], which was hydrogenolyzed over Pd/C to give the antiviral agent **famciclovir** [I; X = H, Ra = Rb = Ac]. Another antiviral agent, penciclovir, was **prepared** similarly.

IT **104227-87-4P**, **Famciclovir**
RL: SPN (Synthetic preparation); PREP (Preparation)
(**preparation** of antiviral purine derivs.)

RN 104227-87-4 CAPLUS

CN 1,3-Propanediol, 2-[2-(2-amino-9H-purin-9-yl)ethyl]-, diacetate (ester) (9CI) (CA INDEX NAME)



L5 ANSWER 51 OF 66 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:339471 CAPLUS
DOCUMENT NUMBER: 122:230755

Prepared by: Mary Hale @2-2507 Rem Bldg 1D86

TITLE: Method of combating acyclovir-resistant herpes simplex viral infections using peptide derivatives, and preparation of the peptide derivatives
INVENTOR(S): Chafouleas, James Gus; Deziel, Robert
PATENT ASSIGNEE(S): Bio-Mega/Boehringer Ingelheim Research Inc., Can.
SOURCE: PCT Int. Appl., 72 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9425046	A1	19941110	WO 1994-CA242	19940429
W: AU, BR, BY, CN, CZ, FI, HU, JP, KR, NO, NZ, PL, RU, SK, UA				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2095408	AA	19941104	CA 1993-2095408	19930503
AU 9466423	A1	19941121	AU 1994-66423	19940429
AU 683465	B2	19971113		
BR 9406575	A	19960319	BR 1994-6575	19940429
CN 1126438	A	19960710	CN 1994-192662	19940429
HU 73779	A2	19960930	HU 1995-3135	19940429
JP 08509476	T2	19961008	JP 1994-523705	19940429
EP 767671	A1	19970416	EP 1994-914991	19940429
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
NO 9504390	A	19960102	NO 1995-4390	19951102

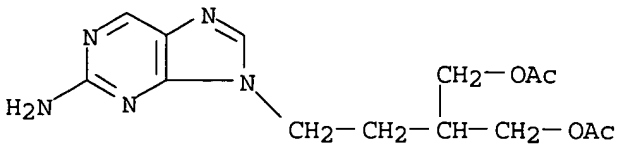
PRIORITY APPLN. INFO.: CA 1993-2095408 A 19930503
WO 1994-CA242 W 19940429

OTHER SOURCE(S): MARPAT 122:230755

AB A method is disclosed for treating acyclovir-resistant herpes infections in a mammal. The method comprises administering a peptide derivative (Markush included), or a combination of the peptide derivative and an antiviral nucleoside analog, to the infected mammal. Peptide derivative preparation, as well as preparation of intermediates, is included. Results demonstrated that a peptide derivative of the invention was active against wild-type HSV-1 and exhibited similar efficacy against acyclovir-resistant HSV-1. Data for synergism (with acyclovir) are also presented.

IT **104227-87-4**, **Famciclovir 104227-87-4D**, **Famciclovir**, peptide derivative mixts.
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(acyclovir-resistant herpes simplex infection treatment with peptide derivs. with optional antiviral nucleoside analog, and **preparation** of the peptide derivs.)

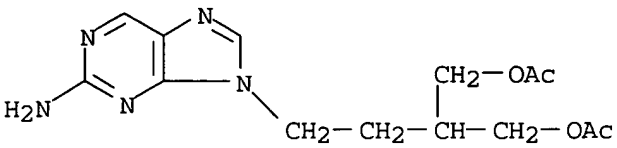
RN 104227-87-4 CAPLUS
CN 1,3-Propanediol, 2-[2-(2-amino-9H-purin-9-yl)ethyl]-, diacetate (ester) (9CI) (CA INDEX NAME)



RN 104227-87-4 CAPLUS
CN 1,3-Propanediol, 2-[2-(2-amino-9H-purin-9-yl)ethyl]-, diacetate (ester)

Prepared by: Mary Hale @2-2507 Rem Bldg 1D86

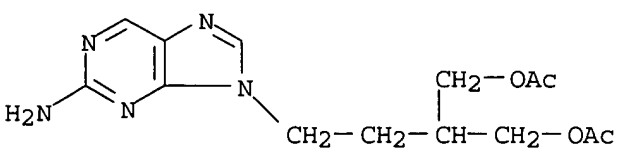
(9CI) (CA INDEX NAME)



L5 ANSWER 52 OF 66 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1994:435199 CAPLUS
DOCUMENT NUMBER: 121:35199
TITLE: Process for the preparation of 2-amino-6-chloropurine
INVENTOR(S): Hanson, John Christopher
PATENT ASSIGNEE(S): SmithKline Beecham PLC, UK
SOURCE: PCT Int. Appl., 10 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9407892	A1	19940414	WO 1993-GB2027	19930928
W: JP, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 662970	A1	19950719	EP 1993-921023	19930928
R: BE, CH, DE, FR, GB, IT, LI, NL				
JP 08502055	T2	19960305	JP 1993-508838	19930928
PRIORITY APPLN. INFO.:			GB 1992-20585 A	19920930
			WO 1993-GB2027 W	19930928

OTHER SOURCE(S): CASREACT 121:35199
AB A process for the **preparation** of 2-amino-6-chloropurine is claimed. The process comprises imidazole ring closure of 2,4,5-triamino-6-chloropyrimidine. The title compound is an intermediate for **famciclovir** [2-[2-(2-amino-9H-purin-9-yl)ethyl]-1,3-propanediol] or penciclovir [2-amino-1,9-dihydro-9-[4-hydroxy-3-(hydroxymethyl)butyl]-6H-purin-6-one].
IT **104227-87-4P, Famciclovir**
RL: SPN (Synthetic preparation); PREP (Preparation)
(**preparation** of)
RN 104227-87-4 CAPLUS
CN 1,3-Propanediol, 2-[2-(2-amino-9H-purin-9-yl)ethyl]-, diacetate (ester) (9CI) (CA INDEX NAME)



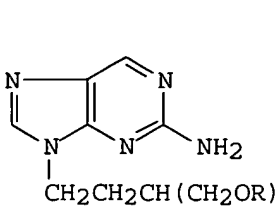
L5 ANSWER 53 OF 66 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1993:190109 CAPLUS

DOCUMENT NUMBER: 118:190109
TITLE: Process for the preparation of 2-acetoxy-methyl-1,4-butanediole-1-acetate from the triacetate with an immobilized hydrolase
INVENTOR(S): Sime, John Thomas; Woroniecki, Stefan Roland; Grinter, Trevor John
PATENT ASSIGNEE(S): Beecham Group PLC, UK
SOURCE: PCT Int. Appl., 15 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

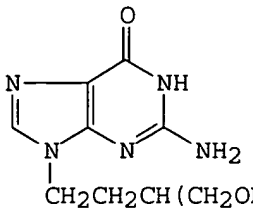
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9303166	A1	19930218	WO 1991-GB1315	19910801
W: BR, CS, FI, HU, NO, PL				
CN 1070002	A	19930317	CN 1991-108598	19910831
PRIORITY APPLN. INFO.:			WO 1991-GB1315	19910801

AB The compound 2-acetoxy-methyl-1,4-butanediole-1-acetate (I) that is an intermediate in the synthesis of the antiviral compds. penciclovir and **famciclovir** is manufactured from the triacetate by regioselective hydrolysis. The hydrolysis is performed using an immobilized hydrolase or immobilized cells containing the hydrolase. A partially purified esterase from homogenates of mycelium of Penicillium frequentans IMI 92265 was **prepared** by (NH4)2SO4 precipitation and ion-exchange chromatog. An aqueous soln of the triacetate of I 4 mg.mL-1 125 μL was mixed with the enzyme **preparation** 250 μL and 4M ammonium sulfate 125 μL and incubated at 20° for 4 h to achieve 97% hydrolysis with a ratio of the desired product to its regioisomer of 95:5. Immobilization of the enzyme on activated Sepharose and its use in an enzyme reactor is demonstrated.

L5 ANSWER 54 OF 66 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1993:160573 CAPLUS
DOCUMENT NUMBER: 118:160573
TITLE: Evidence that famciclovir (BRL 42810) and its associated metabolites do not inhibit the 6β-hydroxylation of testosterone in human liver microsomes
AUTHOR(S): Harrell, A. W.; Wheller, S. M.; Pennick, M.; Clarke, S. E.; Chenery, R. J.
CORPORATE SOURCE: Dep. Drug Metab. Pharmacokinet., SmithKline Beecham, The Frythe/Welwyn/Herts, UK
SOURCE: Drug Metabolism and Disposition (1993), 21(1), 18-23
CODEN: DMDSAI; ISSN: 0090-9556
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I, R=Ac
III, R=H



II

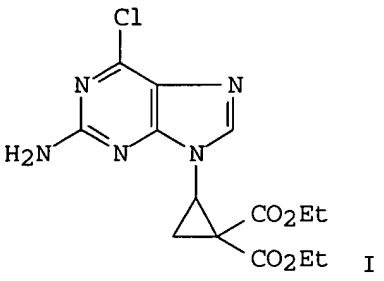
AB **Famciclovir** (I) is the diacetyl 6-deoxy analog of the active antiviral compound penciclovir (II) with potential use in the treatment of infections caused by the herpes family of viruses. The major pathway of metabolism of I is deacetylation to BRL 42359 (III) followed by oxidation to II.

It is possible that I may be coadministered with cyclosporin A to combat viral infections induced by immunosuppression in organ transplant and bone marrow transplant patients. As a result, information is required on possible interactions between the cytochrome P 450 3A substrate cyclosporin A and I and its metabolites in humans. In order to probe cytochrome P 450 3A activity, testosterone 6β-hydroxylation in two human liver microsomal **prepns.** was measured. Nicardipine and ketoconazole, two drugs with known inhibitory interactions with cyclosporin A, were used as pos. controls. Profiles of 6β-hydroxytestosterone production showed no inhibition effected by I, II, or III when marked inhibition was observed in incubations containing nicardipine, nifedipine, or ketoconazole. Further incubations of [14C]BRL 42359 with human liver cytosol and microsomes indicated that III is oxidized to II in cytosol but not in microsomes and that this reaction was not dependent on the presence of NADPH. Because P 450 resides mainly in the microsomal fraction and is dependent on the presence of cofactors for catalytic activity, it seems that this oxidation is not catalyzed by cytochrome P 450. Evidence has, therefore, been gathered to show that I, II, and III are not inhibitors of cytochrome P 450 3A and are, therefore, unlikely to result in metabolic interactions with cyclosporin A or other P 450 3A substrates in vivo.

L5 ANSWER 55 OF 66 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:	1992:612870 CAPLUS
DOCUMENT NUMBER:	117:212870
TITLE:	Regiospecific Michael additions with 2-aminopurines
AUTHOR(S):	Geen, Graham R.; Kincey, Peter M.; Choudary, Bernadette M.
CORPORATE SOURCE:	SmithKline Beecham Pharm., Pinnacles/Harlow/Essex, CM19 5AD, UK
SOURCE:	Tetrahedron Letters (1992), 33(32), 4609-12 CODEN: TELEAY; ISSN: 0040-4039
DOCUMENT TYPE:	Journal
LANGUAGE:	English
OTHER SOURCE(S):	CASREACT 117:212870

GI



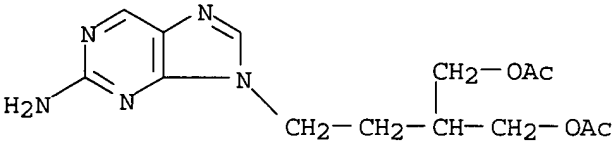
I

AB N-9-Alkylated materials are the sole products obtained from reaction of 2-aminopurines (potential guanine precursors) with Michael acceptors for an extended period of time. Thus, 2-amino-6-chloropurine was treated with ClCH2CH:C(CO2Et)2 to give the cyclopropane derivative I which was converted to famciclovir by reduction in 2 steps.

IT **104227-87-4P, Famciclovir**
RL: SPN (Synthetic preparation); PREP (Preparation)
(regioselective Michael reaction in **preparation** of)

RN 104227-87-4 CAPLUS

CN 1,3-Propanediol, 2-[2-(2-amino-9H-purin-9-yl)ethyl]-, diacetate (ester) (9CI) (CA INDEX NAME)



L5 ANSWER 56 OF 66 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1992:39778 CAPLUS

DOCUMENT NUMBER: 116:39778

TITLE: Manufacture of 3-acetoxymethyl-4-acetoxybutanol from the triacetate with a microbial hydrolase

INVENTOR(S): Grinter, Trevor John; Sime, John Thomas; Woroniecki, Stefan Roland

PATENT ASSIGNEE(S): Beecham Group PLC, UK

SOURCE: PCT Int. Appl., 16 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9113162	A1	19910905	WO 1991-GB275	19910221
W: AU, CA, JP, KR, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				
CA 2076628	AA	19910902	CA 1991-2076628	19910221
AU 9173362	A1	19910918	AU 1991-73362	19910221
AU 645543	B2	19940120		
EP 518902	A1	19921223	EP 1991-904921	19910221

Prepared by: Mary Hale @2-2507 Rem Bldg 1D86

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE

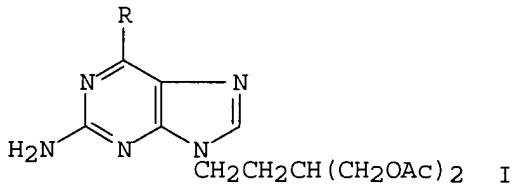
JP 05503428	T2	19930610	JP 1991-505507		19910221
ZA 9101435	A	19920129	ZA 1991-1435		19910227
PRIORITY APPLN. INFO.:			GB 1990-4647	A	19900301
			WO 1991-GB275	A	19910221

OTHER SOURCE(S): CASREACT 116:39778

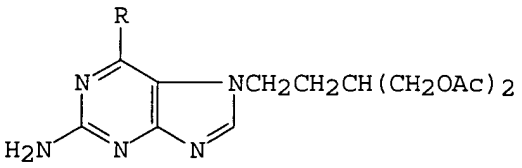
AB The title compound (I) is manufactured from 3-acetoxymethyl-1,4-diacetoxybutane using a microbial hydrolase. I is used in the manufacture of the antiviral compds. penciclovir and **famciclovir.** The esterase of Penicillium frequentans, either in solution or immobilized on Sepharose or Phenyl-Sepharose, was used to **prepare** I.

L5 ANSWER 57 OF 66 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1991:43461 CAPLUS
DOCUMENT NUMBER: 114:43461
TITLE: The effect of the C-6 substituent on the regioselectivity of N-alkylation of 2-aminopurines
AUTHOR(S): Geen, Graham R.; Grinter, Trevor J.; Kincey, Peter M.; Jarvest, Richard L.
CORPORATE SOURCE: Biosci. Res. Cent., Beecham Pharm. Res. Div., Epsom/Surrey, KT18 5XQ, UK
SOURCE: Tetrahedron (1990), 46(19), 6903-14
CODEN: TETRAB; ISSN: 0040-4020
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

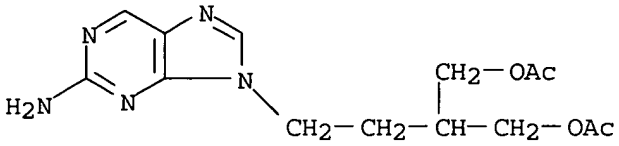


II

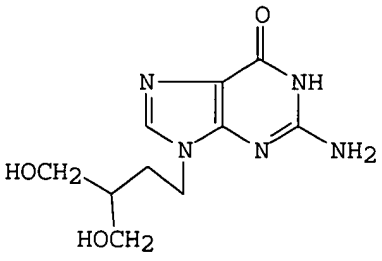
AB 6-Substituted 2-aminopurines were N-alkylated with 2-actoxymethyl-4-iodobutyl acetate. The ratio of N-9 (I) to N-7 (II, R = H, OMe, SMe, F, Cl, Br, iodo, Me, Et, CF3, CHMe2) varied from 1.8:1 to 25:1. The log of this ratio correlated with a combination of resonance and lipopohilicity parameters of the C-6 substituent of the purine.

IT **104227-87-4P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(**preparation** of)

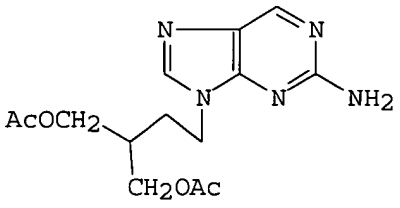
RN 104227-87-4 CAPLUS
CN 1,3-Propanediol, 2-[2-(2-amino-9H-purin-9-yl)ethyl]-, diacetate (ester) (9CI) (CA INDEX NAME)



L5 ANSWER 58 OF 66 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1991:24465 CAPLUS
DOCUMENT NUMBER: 114:24465
TITLE: **Crystal** and molecular structures of the antiviral acyclonucleoside 9-[4-hydroxy-3-(hydroxymethyl)butyl]guanine (BRL 39123, penciclovir) and its prodrug 9-[4-acetoxy-3-(acetoxymethyl)butyl]-2-aminopurine (BRL 42810, **famciclovir**)
AUTHOR(S): Harnden, Michael R.; Jarvest, Richard L.; Slawin, Alexandra M. Z.; Williams, David J.
CORPORATE SOURCE: Biosci. Res. Cent., Beecham Pharm. Res. Div., Epsom/Surrey, KT18 5XQ, UK
SOURCE: Nucleosides & Nucleotides (1990), 9(4), 499-513
CODEN: NUNUD5; ISSN: 0732-8311
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



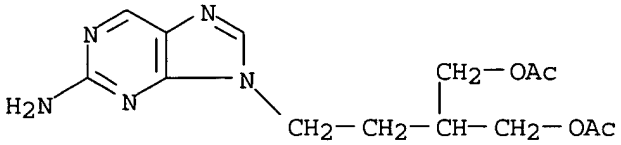
I



II

AB The crystal and mol. structures of acyclonucleosides related antiviral purine derivs. are reported. In I the plane of the acyclic N9 substituent is orthogonal to the purine ring, and there is an intermol. hydrogen bonds. In II characteristic changes in the geometry of the pyrimidine ring in comparison with I are observed In crystals of II there is an absence of major hydrogen bonding interactions and there are π-π interactions between parallel overlapping pyrimidine moieties.

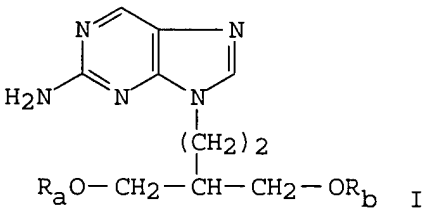
IT **104227-87-4P**
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(**preparation** and mol. structure of)
RN 104227-87-4 CAPLUS
CN 1,3-Propanediol, 2-[2-(2-amino-9H-purin-9-yl)ethyl]-, diacetate (ester) (9CI) (CA INDEX NAME)



L5 ANSWER 59 OF 66 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1990:591061 CAPLUS
DOCUMENT NUMBER: 113:191061
TITLE: Preparation of 9-N-substituted 6-deoxyguanidines as virucides
INVENTOR(S): Geen, Graham Richard; Hanson, John Christopher
PATENT ASSIGNEE(S): Beecham Group PLC, UK
SOURCE: Eur. Pat. Appl., 16 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 369583	A1	19900523	EP 1989-309463	19890918
EP 369583	B1	19950215		
R: BE, CH, DE, ES, FR, GB, GR, IT, LI, NL				
ES 2067549	T3	19950401	ES 1989-309463	19890918
US 5138057	A	19920811	US 1989-409526	19890919
JP 02121992	A2	19900509	JP 1989-242404	19890920
JP 3089354	B2	20000918		
PRIORITY APPLN. INFO.:			GB 1988-22236 A	19880921
OTHER SOURCE(S):	MARPAT 113:191061			

GI



I

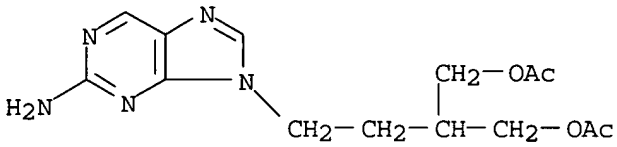
AB Virucidal (no data) purine derivs. I, e.g., **famciclovir** (I; Ra = Rb = Ac) (II), were **prepared** by the title process comprising 9-N-alkylation of 2-amino-6,8-dichloropurine (III) with haloalkyl compds. R1R2R3C(CH2)2L (R1, R3 = protected hydroxymethyl, acyloxymethyl, or groups convertible to hydroxymethyl or acyloxymethyl; R2 = H, a group convertible to H; L = leaving group) followed by the replacement of the 6- and 8-chloro substituents by H and by optional transformations of R1, R3, and of 2-amino group. The yields were higher than in the known process of **preparing** II by a similar alkylation of 2-amino-6-chloro-homolog of III. Thus, a mixture of 22.5 g guanine, 88 g Et3MeN+ Cl-, and SOCl2 was slowly stirred, heated to 50-70° over 0.5 h and kept at 70° for a further 0.5 h to give 28.5 g 8-chloroguanine containing 14.1% H2O. The

latter was converted to its hydrochloride, vacuum dried over P2O5, and added (2.04 g) a solution of 6.6 g Et3MeN+ Cl- in 11 mL MeCN, POCl3 (5.6 mL) was then added to the mixture and the whole was heated 1 h to 60° to give 1.78 g III. A mixture of 5.8 g III, 9.4 g AcOCH2CH(CH2OAc)CH2CH2I, and 5.9 g K2CO3 in 100 mL DMF was stirred at room temperature overnight to give 4.7 g product which (3.9 g) was hydrogenated at 50 psi in the presence of 5% Pd on charcoal to give 2.4 g II. A mixture of 5.8 g III, 9.4 g AcOCH2CH(CH2Ac)CH2CH2I, and 5.9 g K2CO3 in 100 mL DMF was stirred at room temperature overnight to give 4.7 g product which (3.9 g) was hydrogenated at 50 psi in the presence of 5% Pd on charcoal to give 2.4 g II.

IT **104227-87-4P**, **Famciclovir**
RL: SPN (Synthetic preparation); PREP (Preparation)
(**preparation** of)

RN 104227-87-4 CAPLUS

CN 1,3-Propanediol, 2-[2-(2-amino-9H-purin-9-yl)ethyl]-, diacetate (ester) (9CI) (CA INDEX NAME)



L5 ANSWER 60 OF 66 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1990:440718 CAPLUS
DOCUMENT NUMBER: 113:40718
TITLE: Preparation of 2-aminopurine by hydrogenolysis of 2-amino-6-chloropurine in aqueous base over palladium on charcoal
INVENTOR(S): Kincey, Peter Markham
PATENT ASSIGNEE(S): Beecham Group PLC, UK
SOURCE: Eur. Pat. Appl., 6 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 355986	A1	19900228	EP 1989-307268	19890718
EP 355986	B1	19940427		
R: BE, CH, DE, ES, FR, GB, IT, LI, NL				
US 5066805	A	19911119	US 1989-381584	19890718
ES 2053999	T3	19940801	ES 1989-307268	19890718
JP 02073087	A2	19900313	JP 1989-187210	19890719
JP 2825132	B2	19981118		

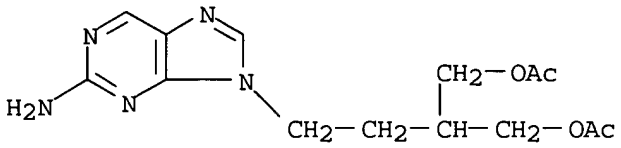
PRIORITY APPLN. INFO.: GB 1988-17270 A 19880720

AB 2-Aminopurine (I) was prepared by catalytic-reduction of 2-amino-6-chloropurine (II) using Pd/C in aqueous base (NaOH) at .apprx.50° and 70 kPa H. Thus, 0.5 mol II in 500 mL H2O containing 50 g NaOH was hydrogenated over 10 g 5% Pd/C at 100 psi and 50° for 3 h to give 83% I. A mixture of I, (MeCO2CH2)2CHCH2CH2I, and K2CO3 in DMF was stirred 18 h at room temperature to give 58% of the antiviral BRL 42810.

IT **104227-87-4P**, BRL 42810

Prepared by: Mary Hale @2-2507 Rem Bldg 1D86

RL: SPN (Synthetic preparation); PREP (Preparation)
(**preparation** of)
RN 104227-87-4 CAPLUS
CN 1,3-Propanediol, 2-[2-(2-amino-9H-purin-9-yl)ethyl]-, diacetate (ester) (9CI) (CA INDEX NAME)



L5 ANSWER 61 OF 66 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1990:440345 CAPLUS
DOCUMENT NUMBER: 113:40345
TITLE: Preparation of purine derivatives as virucides
INVENTOR(S): Grinter, Trevor John; Kincey, Peter Markham
PATENT ASSIGNEE(S): Beecham Group PLC, UK
SOURCE: Eur. Pat. Appl., 19 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 352953	A2	19900131	EP 1989-307271	19890718
EP 352953	A3	19911023		
EP 352953	B1	20010103		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
AT 198479	E	20010115	AT 1989-307271	19890718
ES 2153343	T3	20010301	ES 1989-307271	19890718
DK 8903626	A	19900124	DK 1989-3626	19890721
DK 171991	B1	19970908		
FI 8903535	A	19900124	FI 1989-3535	19890721
NO 8902998	A	19900124	NO 1989-2998	19890721
NO 169008	B	19920120		
NO 169008	C	19920429		
AU 8938822	A1	19900125	AU 1989-38822	19890721
AU 623667	B2	19920521		
JP 02059583	A2	19900228	JP 1989-190386	19890721
JP 2856773	B2	19990210		
HU 50820	A2	19900328	HU 1989-3709	19890721
HU 204829	B	19920228		
ZA 8905567	A	19900725	ZA 1989-5567	19890721
US 5017701	A	19910521	US 1989-383859	19890721
PL 161207	B1	19930630	PL 1989-280709	19890721
KR 137468	B1	19980601	KR 1989-10404	19890722
HK 1012355	A1	20020215	HK 1998-113475	19981215

PRIORITY APPLN. INFO.: GB 1988-17607 A 19880723
OTHER SOURCE(S): MARPAT 113:40345
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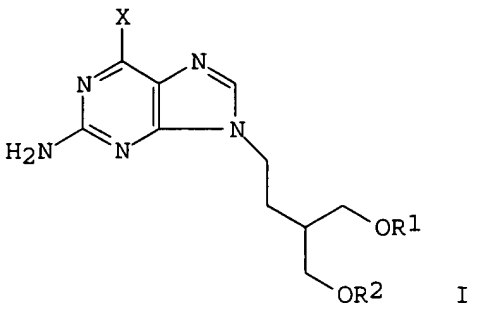


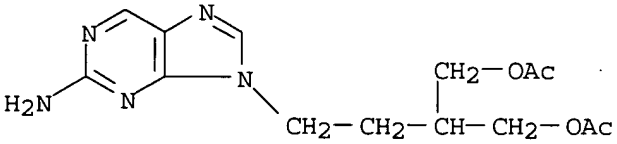
I

AB The title compds. (I; X = H, OH; R1, R2 = H, R3CO; R3 = Ph, alkyl), useful as virucides (no data), were prepared by N-9 alkylation of aminopurines 6-substituted by a leaving group, followed by hydrolysis/hydrogenolysis. Thus, (AcOCH2)2CHCH2CH2I, 2-amino-6-iodopurine, and K2CO3 were stirred 18 h in DMF to give 79.4% I (X = I, R1 = R2 = Ac). The latter was hydrogenated in EtOH over Pd/C to give I (X = H; R1, R2 unchanged).

IT **104227-87-4P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**preparation** of, as virucide)

RN 104227-87-4 CAPLUS

CN 1,3-Propanediol, 2-[2-(2-amino-9H-purin-9-yl)ethyl]-, diacetate (ester) (9CI) (CA INDEX NAME)



L5 ANSWER 62 OF 66 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1990:83948 CAPLUS

DOCUMENT NUMBER: 112:83948

TITLE: Selection of an oral prodrug (BRL 42810; famciclovir) for the antiherpes virus agent BRL 39123 [9-(4-hydroxy-3-hydroxymethylbut-1-yl)guanine; penciclovir]

AUTHOR(S): Hodge, R. Anthony Vere; Sutton, David; Boyd, Malcolm R.; Harnden, Michael R.; Jarvest, Richard L.

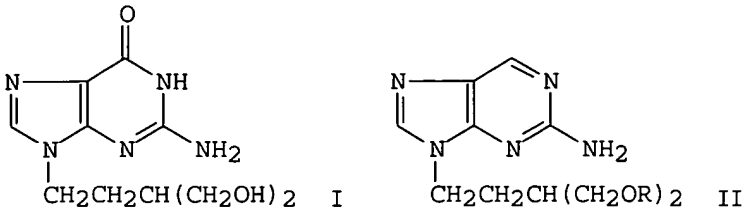
CORPORATE SOURCE: Biosci. Res. Cent., Beecham Pharm. Res. Div., Great Burgh/Epxom/Surrey, KT18 5XQ, UK

SOURCE: Antimicrobial Agents and Chemotherapy (1989), 33(10), 1765-73
CODEN: AMACCQ; ISSN: 0066-4804

DOCUMENT TYPE: Journal

LANGUAGE: English

GI

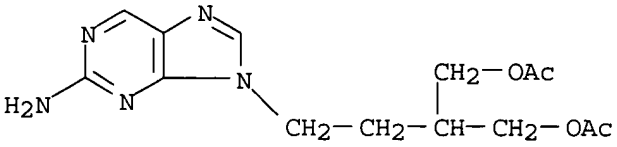


AB The limited oral absorption in rodents of the antiherpes virus agent penciclovir (I) prompted a search for oral prodrugs. The I 6-deoxy derivative [II; R = H (BRL 42359)] and the corresponding diacetyl and dipropionyl 6-deoxy derivs. (II; R = Ac (famciclovir) and R = Et CO (BRL 43599)] were tested as oral prodrugs. The in vivo absorption (dose, 0.2 mmol/kg) and the conversion to the active compound, I, were determined in rats. Compared with the Na salt of I given i.v., the bioavailabilities of I from orally administered I, BRL 42359, famciclovir, and BRL 43599 were 1.5, 9, 41, and 27% resp. These prodrugs and 6-deoxyacyclovir were tested for stability in rat duodenal contents and for metabolism in rat intestinal wall homogenate, liver homogenate, and blood and in the corresponding human fluids and tissues. Famciclovir was much more stable the BRL 43599 in human duodenal contents (half-lives, >2 h and 7 min, resp.) yet was efficiently converted to I by the tissue homogenates. The major metabolic pathway was by deacetylation followed by oxidation at the 6 position. The rate of oxidation was comparable to that of 6-deoxyacyclovir, which is known to be converted efficiently to acyclovir in humans. Famciclovir was selected for further evaluation and progression to studies in humans. These subsequent studies confirmed that, after oral dosing with famciclovir, more than half the dose was absorbed and rapidly converted to I.

IT **104227-87-4P, Famciclovir**
RL: SPN (Synthetic preparation); PREP (Preparation)
(**preparation** and pharmacokinetics of, as penciclovir prodrug)

RN 104227-87-4 CAPLUS

CN 1,3-Propanediol, 2-[2-(2-amino-9H-purin-9-yl)ethyl]-, diacetate (ester) (9CI) (CA INDEX NAME)



L5 ANSWER 63 OF 66 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1989:614873 CAPLUS
Correction of: 1989:458254

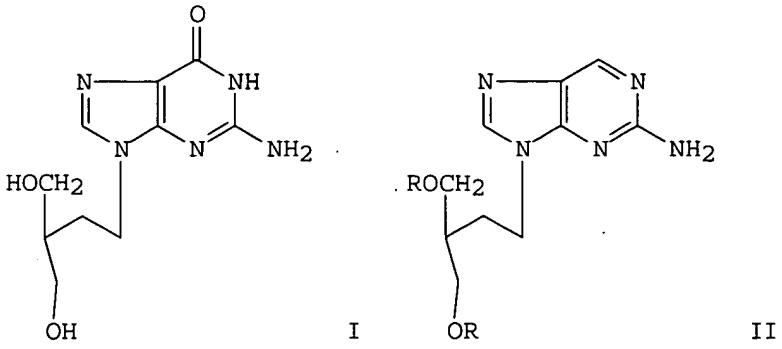
DOCUMENT NUMBER: 111:214873
Correction of: 111:58254

TITLE: Prodrugs of the selective antiherpesvirus agent 9-[4-hydroxy-3-(hydroxymethyl)but-1-yl]guanine (BRL 39123) with improved gastrointestinal absorption properties

AUTHOR(S): Harnden, Michael R.; Jarvest, Richard L.; Boyd, Malcolm R.; Sutton, David; Vere Hodge, R. Anthony

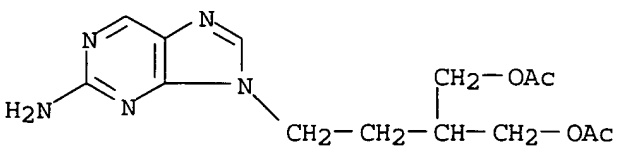
Prepared by: Mary Hale @2-2507 Rem Bldg 1D86

CORPORATE SOURCE: Biosci. Res. Cent., Beecham Pharm. Res. Div., Epsom/Surrey, KT18 5XQ, UK
SOURCE: Journal of Medicinal Chemistry (1989), 32(8), 1738-43
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 111:214873
GI



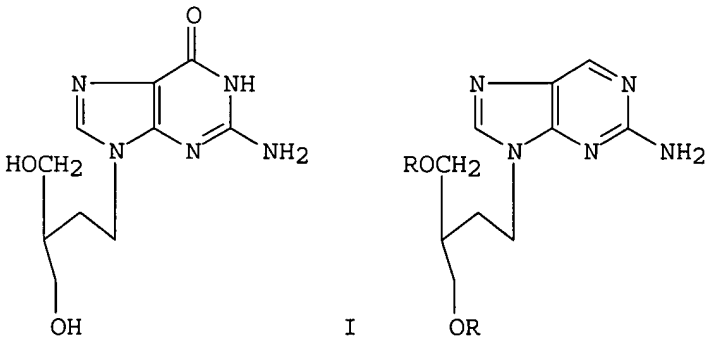
AB Potential oral prodrugs of the anitherpes virus acyclonucleoside 9-[4-hydroxy-3-(hydroxymethyl)but-1-yl]guanine (I,BRL 39123) have been synthesized and evaluated for bioavailability of I in the blood of mice. Reduction of 9-[4-acetoxy-3-(acetoxymethyl)but-1-yl]-2-amino-6-chloropurine with HCO2NH4-Pd afforded the 2-aminopurine II (R = Ac), which was hydrolyzed to the 5'-monoacetate and to 2-amino-9-[4-hydroxy-3-(hydroxymethyl)but-1-yl]purine (II; R = H). II (R = H) was converted to addnl. monoester and diester derivs. and to its di-O-isopropylidene derivative Both II (R = H) and its esters and isopropylidene derivative were well adsorbed after oral administration and converted efficiently to I, II (R = Ac, EtCO) providing concns. of I in the blood that were >15-fold higher than those observed after dosing either I or its esters. Some previously prepared 6-alkoxy-9-[4-hydroxy-3-(hydroxymethyl)but-1-yl]purines also showed improved absorption properties but their conversion to I was less efficient than that of the 2-aminopurine derivs. On the basis of these results and expts. involving detns. of rates of conversion to I in the presence of rat and human tissue prepns., II (R = Ac) (BRL 42810) was identified as the preferred prodrug of I. Oral bioavailability studies in healthy human subjects confirmed II (R = Ac) as an effective prodrug, and this compound is being evaluated in clin. trials.

IT **104227-87-4P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(**preparation** of, prodrug of [hydroxy(hydroxymethyl)butyl]guanine)
RN 104227-87-4 CAPLUS
CN 1,3-Propanediol, 2-[2-(2-amino-9H-purin-9-yl)ethyl]-, diacetate (ester) (9CI) (CA INDEX NAME)



Prepared by: Mary Hale @2-2507 Rem Bldg 1D86

L5 ANSWER 64 OF 66 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1989:458254 CAPLUS
DOCUMENT NUMBER: 111:58254
TITLE: Prodrugs of the selective antiherpesvirus agent 9-[4-hydroxy-3-(hydroxymethyl)but-1-yl]guanine (BRL 39123) with improved gastrointestinal absorption properties
AUTHOR(S): Harnden, Michael R.; Jarvest, Richard L.; Boyd, Malcolm R.; Sutton, David; Hodge, R. Anthony Vere
CORPORATE SOURCE: Biosci. Res. Cent., Beecham Pharm. Res. Div., Epsom/Surrey, KT18 5XQ, UK
SOURCE: Journal of Medicinal Chemistry (1989), 32(8), 1738-43
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 111:58254
GI

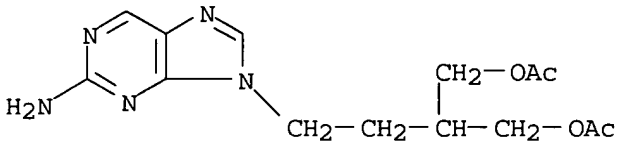


AB Potential oral prodrugs of the antiherpes virus acyclonucleoside 9-[4-hydroxy-3-(hydroxymethyl)but-1-yl]guanine (I, BRL 39123) have been synthesized and evaluated for bioavailability of I in the blood of mice. Reduction of 9-[4-acetoxy-3-(acetoxymethyl)but-1-yl]-2-amino-6-chloropurine with HCO2NH4-Pd afforded the 2-aminopurine II (R = Ac), which was hydrolyzed to the 5'-monoacetate and to 2-amino-9-[4-hydroxy-3-(hydroxymethyl)but-1-yl]purine (II; R = H). II (R = H) was converted to addnl. monoester and diester derivs. and to its di-O-isopropylidene derivative Both II (R = H) and its esters and isopropylidene derivative were well adsorbed after oral administration and converted efficiently to I, II (R = Ac, EtCO) providing concns. of I in the blood that were >15-fold higher than those observed after dosing either I or its esters. Some previously prepared 6-alkoxy-9-[4-hydroxy-3-(hydroxymethyl)but-1-yl]purines also showed improved absorption properties, but their conversion to I was less efficient than that of the 2-aminopurine derivs. On the basis of these results and expts. involving detns. of rates of conversion to I in the presence of rat and human tissue prepns., II (R = Ac) (BRL 42810) was identified as the preferred prodrug of I. Oral bioavailability studies in healthy human subjects confirmed II (R = Ac) as an effective prodrug, and this compound is being evaluated in clin. trials.

IT **104227-87-4P**

Prepared by: Mary Hale @2-2507 Rem Bldg 1D86

RL: SPN (Synthetic preparation); PREP (Preparation)
(**preparation** of, prodrug of [hydroxy(hydroxymethyl)butyl]guanine)
RN 104227-87-4 CAPLUS
CN 1,3-Propanediol, 2-[2-(2-amino-9H-purin-9-yl)ethyl]-, diacetate (ester) (9CI) (CA INDEX NAME)



L5 ANSWER 65 OF 66 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1988:492663 CAPLUS
DOCUMENT NUMBER: 109:92663
TITLE: Preparation of 2-aminopurines as precursors of a guanine virucide
INVENTOR(S): Harnden, Michael Raymond; Jarvest, Richard Lewis
PATENT ASSIGNEE(S): Beecham Group PLC, UK
SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 8705604	A1	19870924	WO 1986-GB153	19860317
W: AT, FI, HU, KR, NO				
AT 8609042	A	19890315	AT 1986-9042	19860317
AT 389118	B	19891025		
HU 47576	A2	19890328	HU 1986-3048	19860317
HU 198934	B	19891228		
FI 8705059	A	19871116	FI 1987-5059	19871116
FI 87564	B	19921015		
FI 87564	C	19930125		
NO 8704764	A	19871116	NO 1987-4764	19871116
NO 167572	B	19910812		
NO 167572	C	19911120		

PRIORITY APPLN. INFO.: WO 1986-GB153 A 19860317
OTHER SOURCE(S): CASREACT 109:92663
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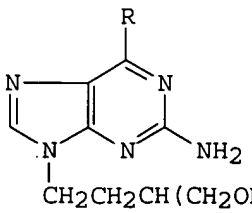


I

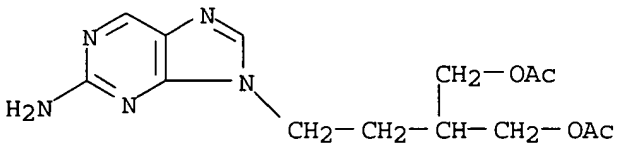
AB The title compds. I (R = H; R1, R2 = H, acyl, phosphoryl; R1R2 = cyclic

acetal, cyclic carbonate, cyclic phosphate) useful as virucides (no data) were prepared by (a) hydrolysis of I in which R1R2 = Me2C; (b) hydrogenolysis of I in which R = Cl; (c) phosphorylating protected-amino I. I (R = Cl, R1R2 = Me2C) was refluxed in EtOH containing Pd/C overnight to give I (R = R1 = R2 = H) which was stirred 16 h with (EtCO)2O in DMF containing 4-(dimethylamino)pyridine to give I (R = H, R1 = R2 = COEt). The latter compound gave a blood concentration of 20 μg/mL 9-(4-hydroxy-3-hydroxymethylbut-1-yl)guanine (II) in mice 15 min after oral gavage compared with 1.1 μg II/mL 15 min after administration of II by itself.

IT **104227-87-4P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(**preparation** of, as guanine virucide precursor)

RN 104227-87-4 CAPLUS

CN 1,3-Propanediol, 2-[2-(2-amino-9H-purin-9-yl)ethyl]-, diacetate (ester) (9CI) (CA INDEX NAME)



L5 ANSWER 66 OF 66 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1986:533669 CAPLUS
DOCUMENT NUMBER: 105:133669
TITLE: Aminopurine derivatives
PATENT ASSIGNEE(S): Beecham Group PLC, UK
SOURCE: Jpn. Kokai Tokkyo Koho, 14 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 61085388	A2	19860430	JP 1985-207693	19850919
JP 05086792	B4	19931214		
EP 182024	A2	19860528	EP 1985-111354	19850909
EP 182024	A3	19890308		
EP 182024	B1	19910403		
R: BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
DK 8504246	A	19860321	DK 1985-4246	19850918
DK 167019	B1	19930816		
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CA 1262899	A1	19891114	CA 1985-491028	19850918
ES 547128	A1	19870301	ES 1985-547128	19850919
CZ 283721	B6	19980617	CZ 1991-3915	19911219
JP 06025241	A2	19940201	JP 1993-130044	19930507
JP 08026021	B4	19960313		

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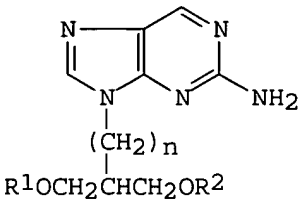


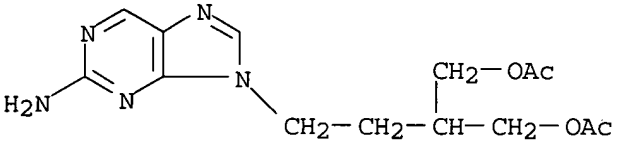
I

AB Title compds. I (R1, R2 = H, acyl, phosphate, etc.) and their salts, useful as virucides (no data), were prepared Thus, refluxing 0.54 g 2-amino-6-chloro-9-chloro-9-[2-(2,2-dimethyl-1,3-dioxan-3-yl)ethyl]purine with 450 mg 10% Pd/C in ethanol and cyclohexane gave 36% 2-amino-9-[4-hydroxy-3-(hydroxymethyl)-but-1-yl]purine.

IT **104227-87-4P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**preparation** of, as virucide)

RN 104227-87-4 CAPLUS

CN 1,3-Propanediol, 2-[2-(2-amino-9H-purin-9-yl)ethyl]-, diacetate (ester) (9CI) (CA INDEX NAME)



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E FAMCICLOVIR/CN 5
L1 1 S E3

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DICTIONARY FILE UPDATES:  10 AUG 2005  HIGHEST RN 859511-21-0

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* the IDE default display format and the ED field has been added,   *
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* available and contains the CA role and document type information. *
*                                                                    *
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Structure search iteration limits have been increased.  See HELP SLIMITS
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Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

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